CDC PUBLIC HEALTH GRAND ROUNDS

Working to Eliminate Measles Around the Globe




June 16, 2015

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

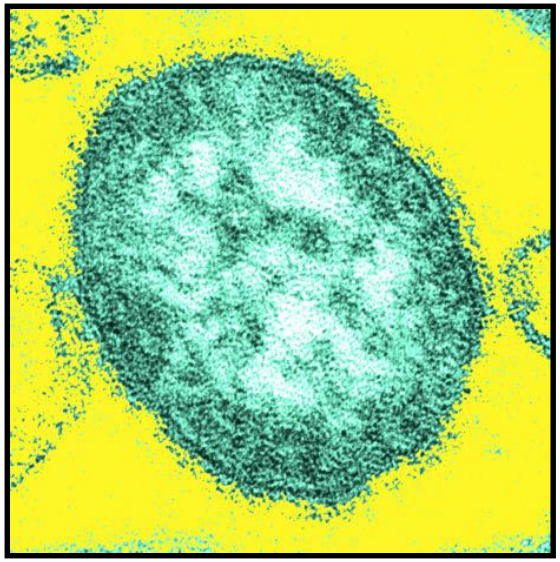
The Measles & Rubella Initiative and Partnerships for Elimination

James L. Goodson, MPH
Senior Measles Scientist
Accelerated Disease Control and
Vaccine-Preventable Diseases Surveillance Branch
Global Immunization Division
Center for Global Health

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Measles Virus

- **RNA virus**
  - Family: Paramyxoviridae
  - Genus: Morbillivirus
- **Humans are the only reservoir**
- **Airborne transmission via aerosolized respiratory secretions from coughing or sneezing**
- **After 7–21 day incubation period, clinical symptoms develop**
- **Accompanied by immunosuppression, often leading to secondary bacterial infections**

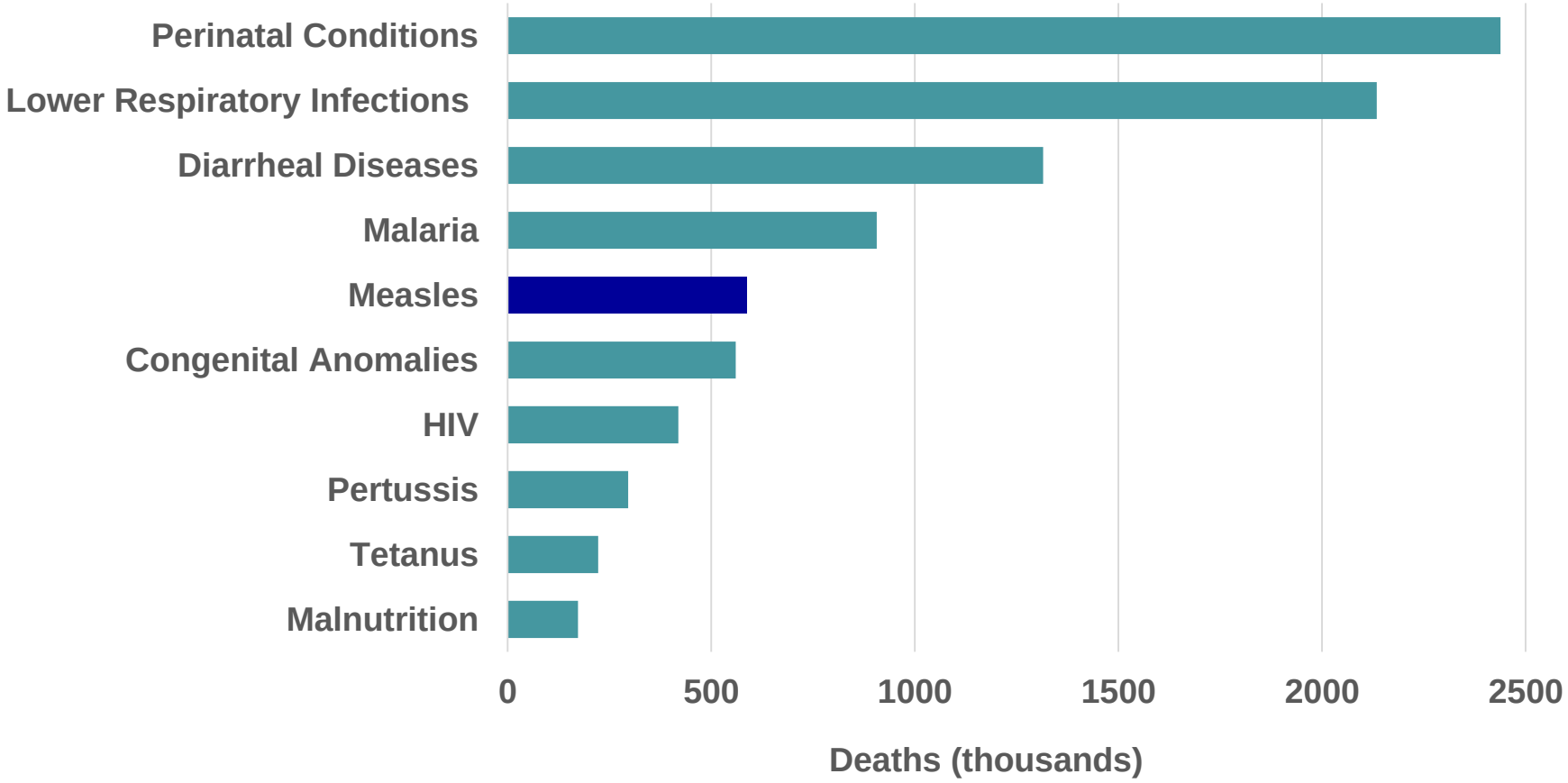


MEASLES DISEASE

Photo courtesy of
Professor Samuel Katz,
Duke University Medical Center

- Highly contagious
- Vaccine preventable
- Typically occurs in childhood
- Classic rash and fever clinical presentation
- Severe complications: pneumonia, diarrhea, encephalitis, death
- Case-fatality ratio: 0.1%–10%

Top Ten Causes of Death Worldwide in Children Under 5 Years, 2000



World Health Organization (WHO), Global Burden of Disease 2000 Project

Measles is Highly Contagious and Prevented by Vaccination

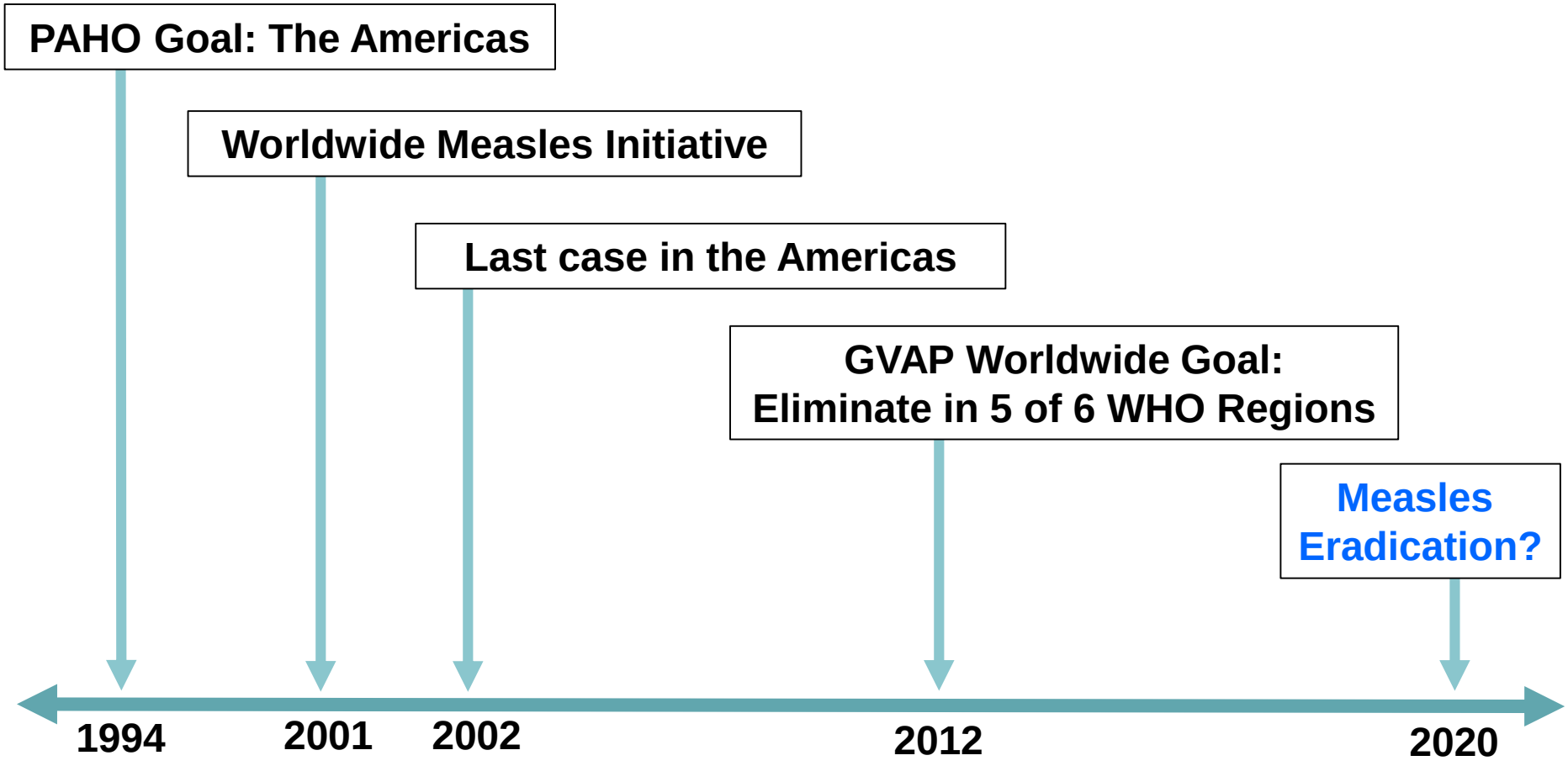
- **Safe and highly effective vaccine**
  - Licensed in 1963
  - Requires cold chain for storage
- **Immunity and vaccination coverage needs to be high**
  - Over 90% to interrupt transmission and prevent epidemics
- **WHO recommends 2 doses for children**
  - 2 doses protects 97%–99% of children
  - 1 dose protects
    - 85% at 9 months
    - ≥95% at 12 months

http://www.who.int/wer/2009/wer8435.pdf

Efforts to Eradicate Smallpox and Polio Support Measles Elimination

- **Smallpox (achieved)**
  - Integrated measles control efforts in 20 West Africa countries
  - Contributed to WHO's Expanded Program on Immunization (EPI)
  - Lives have been saved and resources are able to be directed to other public health priorities
- **Polio (nearly there)**
  - Infrastructure to eradicate polio designed to be integrated with activities to eliminate measles
  - Challenges (e.g., insecurity) have delayed reaching goal
  - Lessons learned from polio can be transferred to MR eradication
  - Much harder than anticipated, but worth the investment
  - The POLIO ENDGAME has begun and in countries that have eliminated polio, assets are being transitioned

“Measles eradication should be done.” World Health Assembly, 2011



PAHO: Pan-American Health Organization
GVAP: Global Vaccine Action Plan

Global Measles Vaccination Targets by 2015

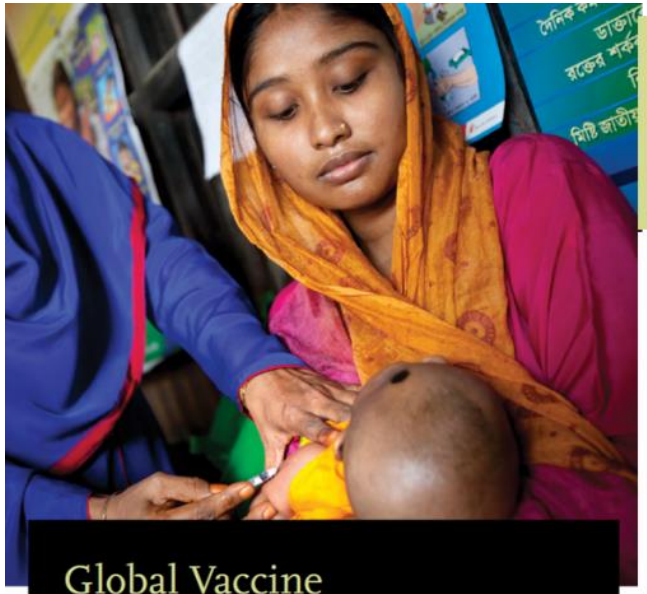
1. **Increase prevention –** Increase measles vaccination coverage for first dose (MCV1)
   - At least 90% nationally and at least 80% at district levels

2. **Decrease disease –** Reduce reported incidence of measles to fewer than 5 cases per million population

3. **Decrease deaths –** Reduce measles mortality 95%, based on number of deaths estimated in 2000

Global Vaccine Action Plan (GVAP) Measles & Rubella Initiative Goals

- Use combined measles and rubella vaccine
- Eliminate measles and rubella in 5 of 6 WHO regions by 2020



Global Vaccine Action Plan

2011–2020

The vision

for the Decade of Vaccines (2011–2020) is of a world in which all individuals and communities enjoy lives free from vaccine-preventable diseases.

Dr. Seth Berkley
Chief Executive Officer
GAVI Alliance

Dr. Margaret Chan
Director General
World Health Organization

Dr. Christopher Elias
President
Global Development Program
Bill & Melinda Gates Foundation

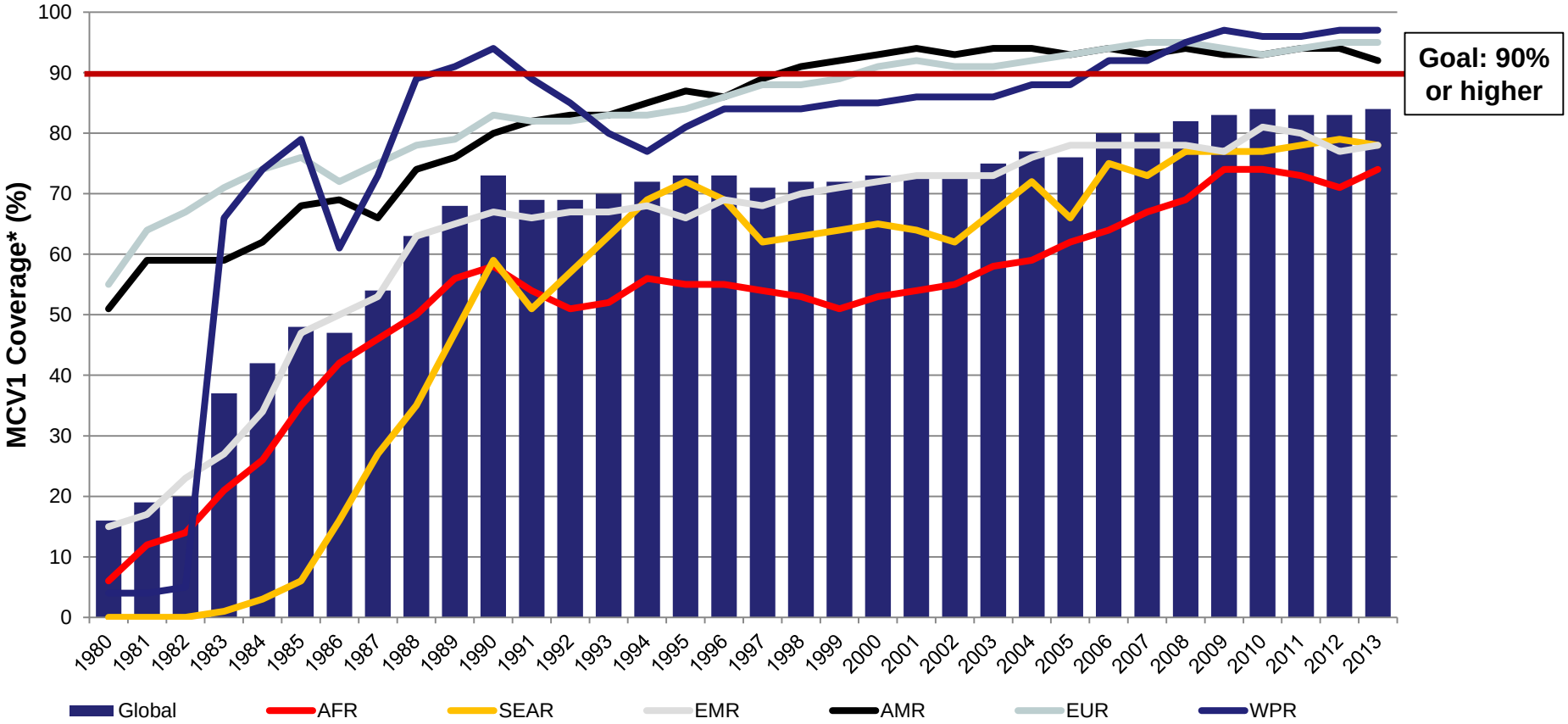
Dr. Anthony Fauci
Director
US National Institute of Allergies and Infectious Diseases

Mr. Anthony Lake
Executive Director
United Nations Children's Fund (UNICEF)

Ms. Joy Phumaphi
Executive Secretary
African Leaders Malaria Alliance

Worldwide Measles First-Dose (MCV1) Vaccination Coverage Stagnating

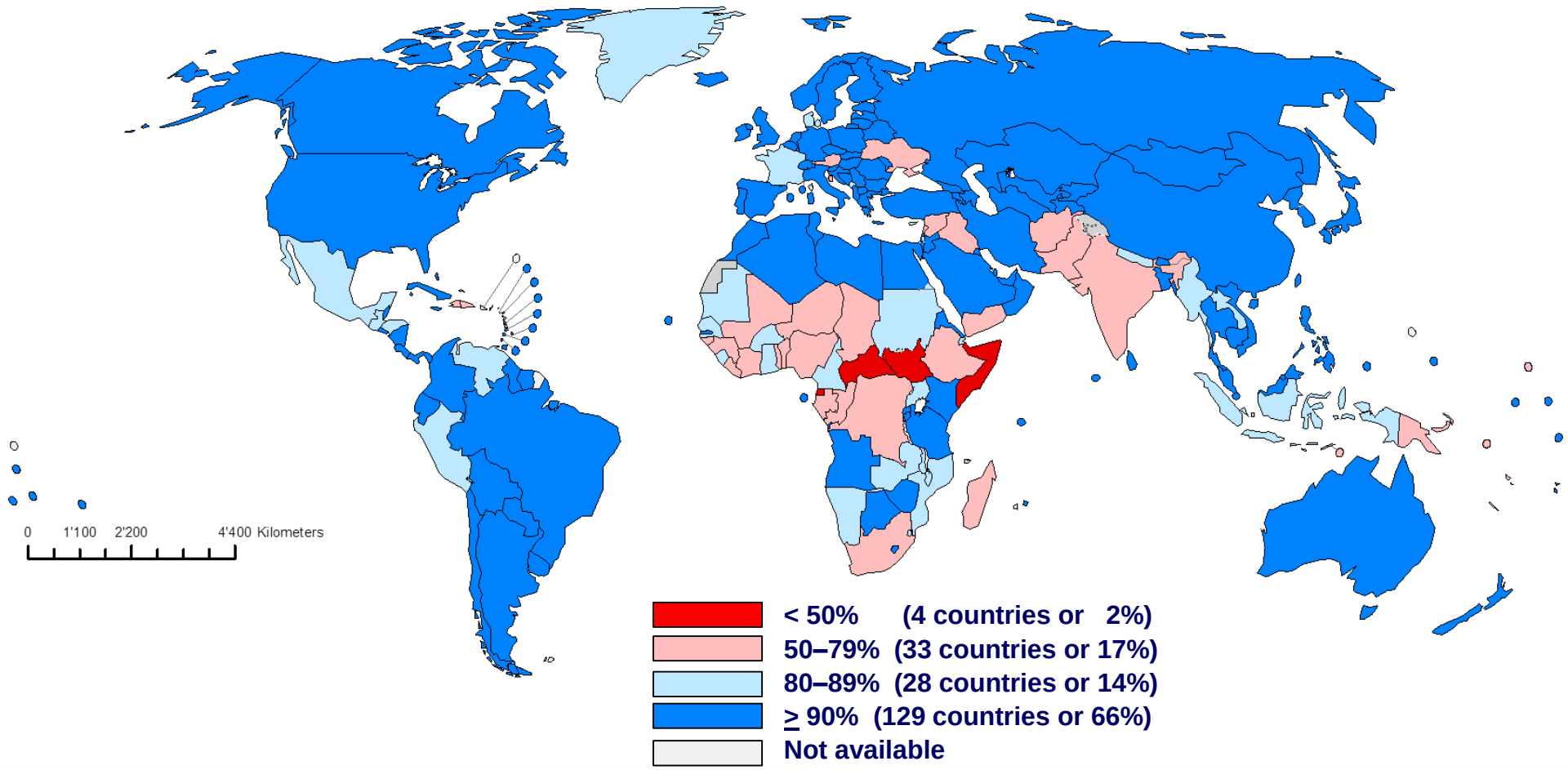
MCV1 Vaccination Coverage by WHO Region



AFR: African region
AMR: Region of the Americas
SEAR: South-East Asia region
EUR: European region
EMR: Eastern Mediterranean region
WPR: Western Pacific region

WHO/UNICEF coverage estimates 2013 revision, July 16, 2014

Measles First-Dose Vaccination (MCV1) Coverage by Country – Goal is 90% or Higher



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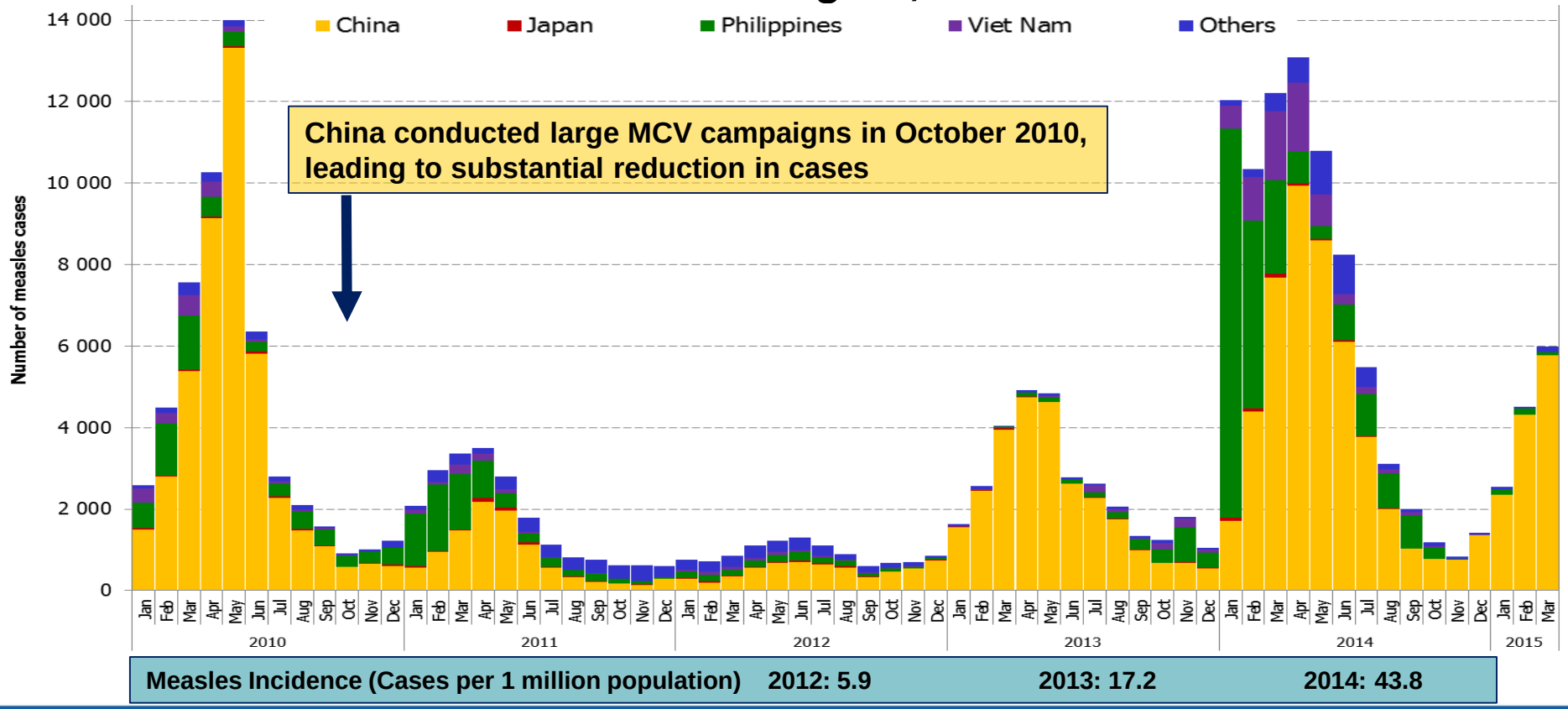
WHO/UNICEF coverage estimates 2013 revision, July 16, 2014

Vaccination Campaigns Are Effective But Sustained Efforts Are Essential

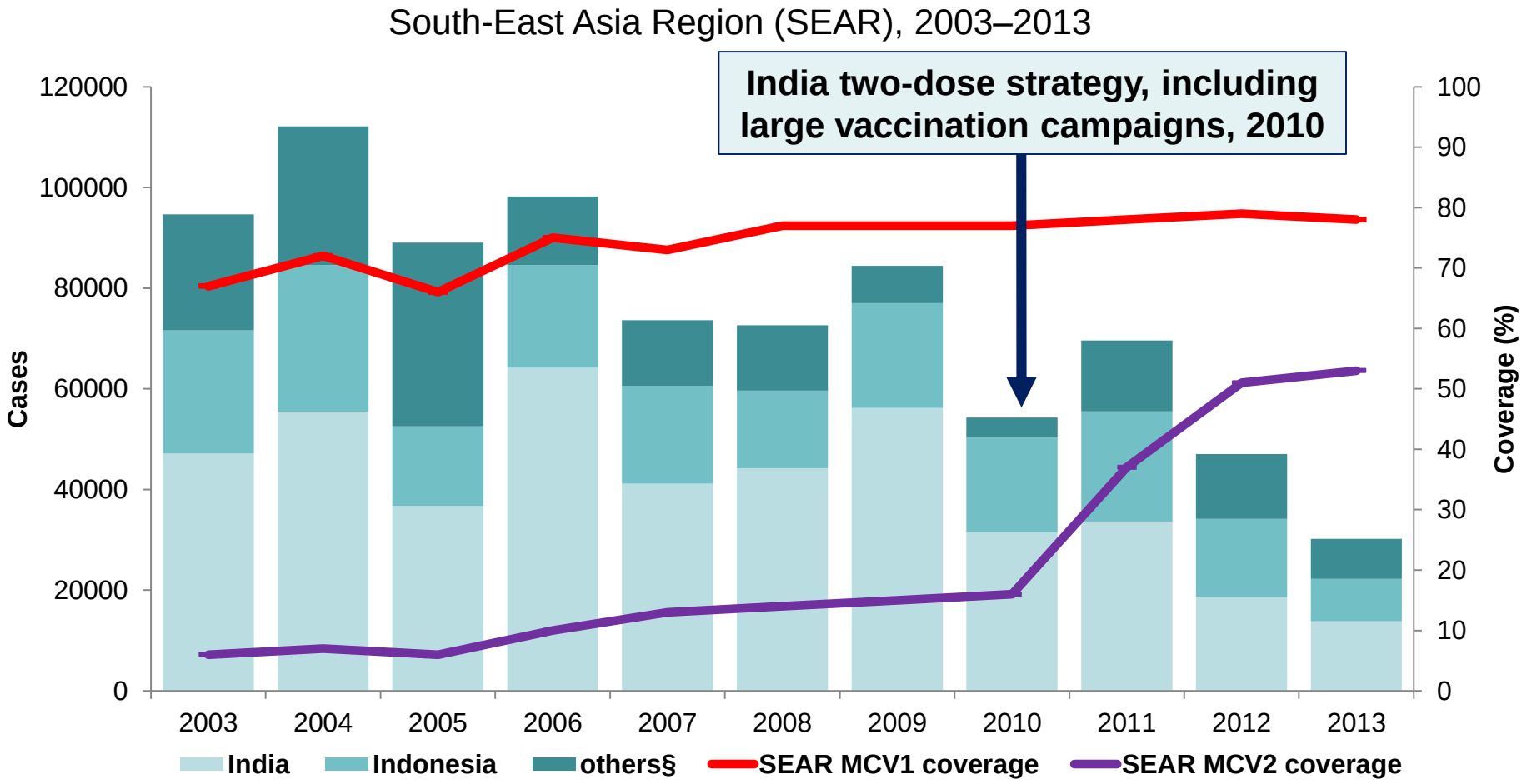
Reported Measles Cases by Month of Onset, Western Pacific Region, 2010–2015



Measles Incidence (Cases per 1 million population) **2012: 5.9** **2013: 17.2** **2014: 43.8**

Measles and rubella monthly country reports to WHO, as of April 20, 2015

Reported Cases of Measles Drop as Measles Second Dose (MCV2) Coverage Increases



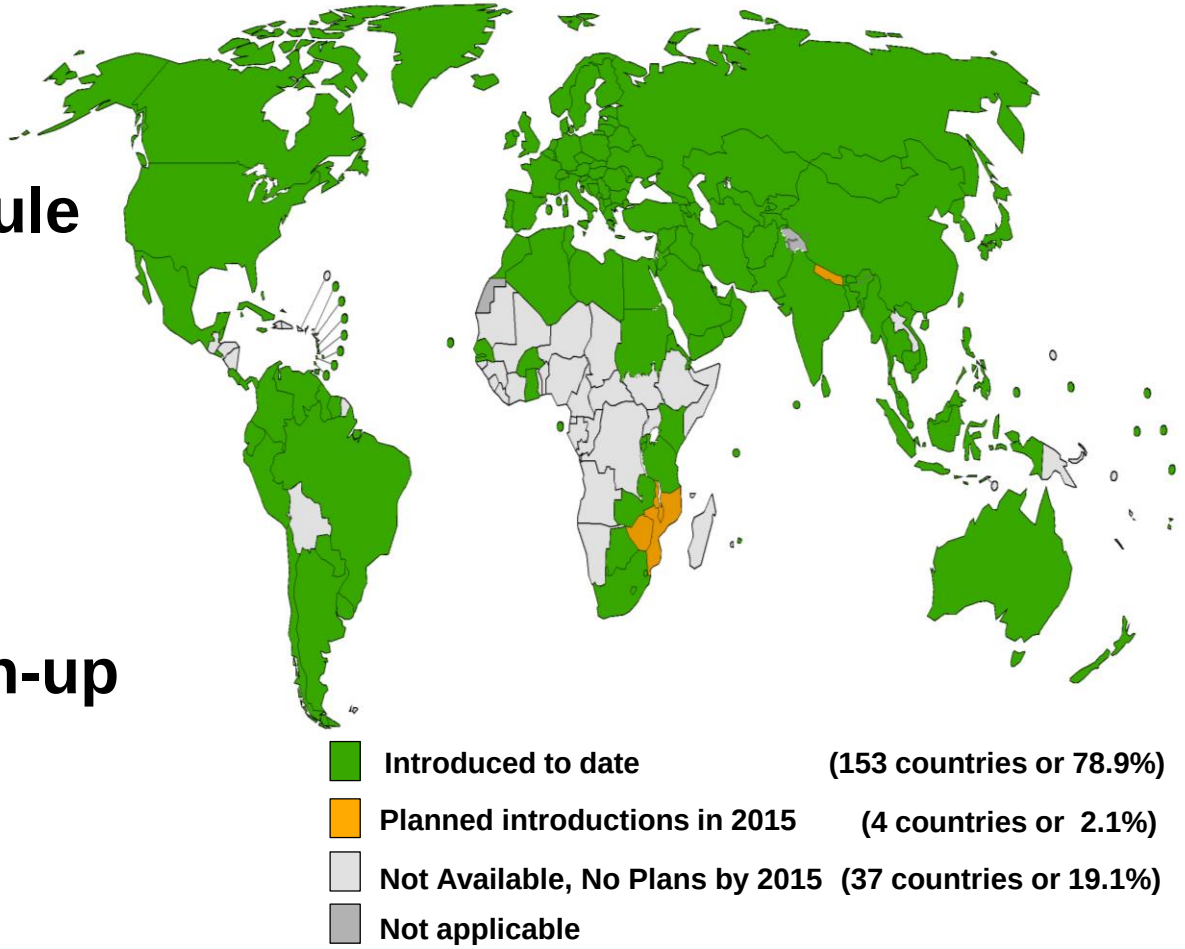
§ Others include Bangladesh, Bhutan, DPR Korea, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste
MCV1: First dose of measles containing vaccine
MMWR 2015;64:613–7

Implementing Measles Second Dose (MCV2)

- **In 2013, global coverage of MCV2 was only 53%**
- **Increasing vaccination efforts can increase two-dose coverage**
  - Routine Immunization (RI) practices
    - As children are born and grow
  - Supplementary Immunization Activities (SIA)
    - Catch-up campaigns to reach large populations and different at-risk age groups
    - Opportunity to provide additional services beyond immunizations

Introducing Measles Second Dose (MCV2) into Routine Immunization Schedule

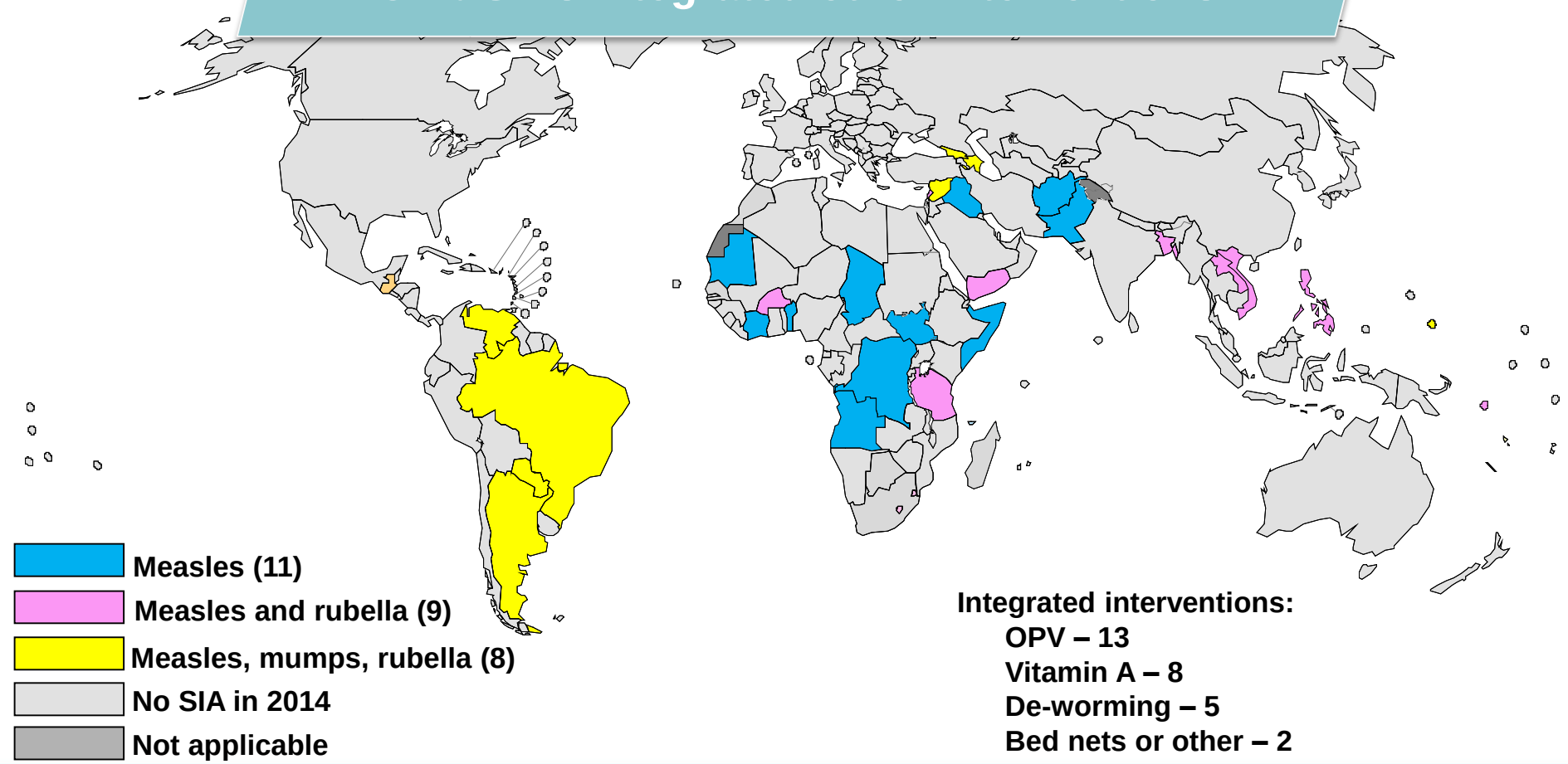
- Each year, more countries introduce MCV2 into RI schedule
- Establishes child health platform for 2nd year of life
- Opportunity to catch-up other vaccines and offer other services



RI: Routine immunizations
Immunization Vaccines and Biologicals, WHO, as of March 5, 2015

43 Measles SIAs in 28 Countries Reached Over 210 Million Children in 2014

81% SIAs integrated other interventions



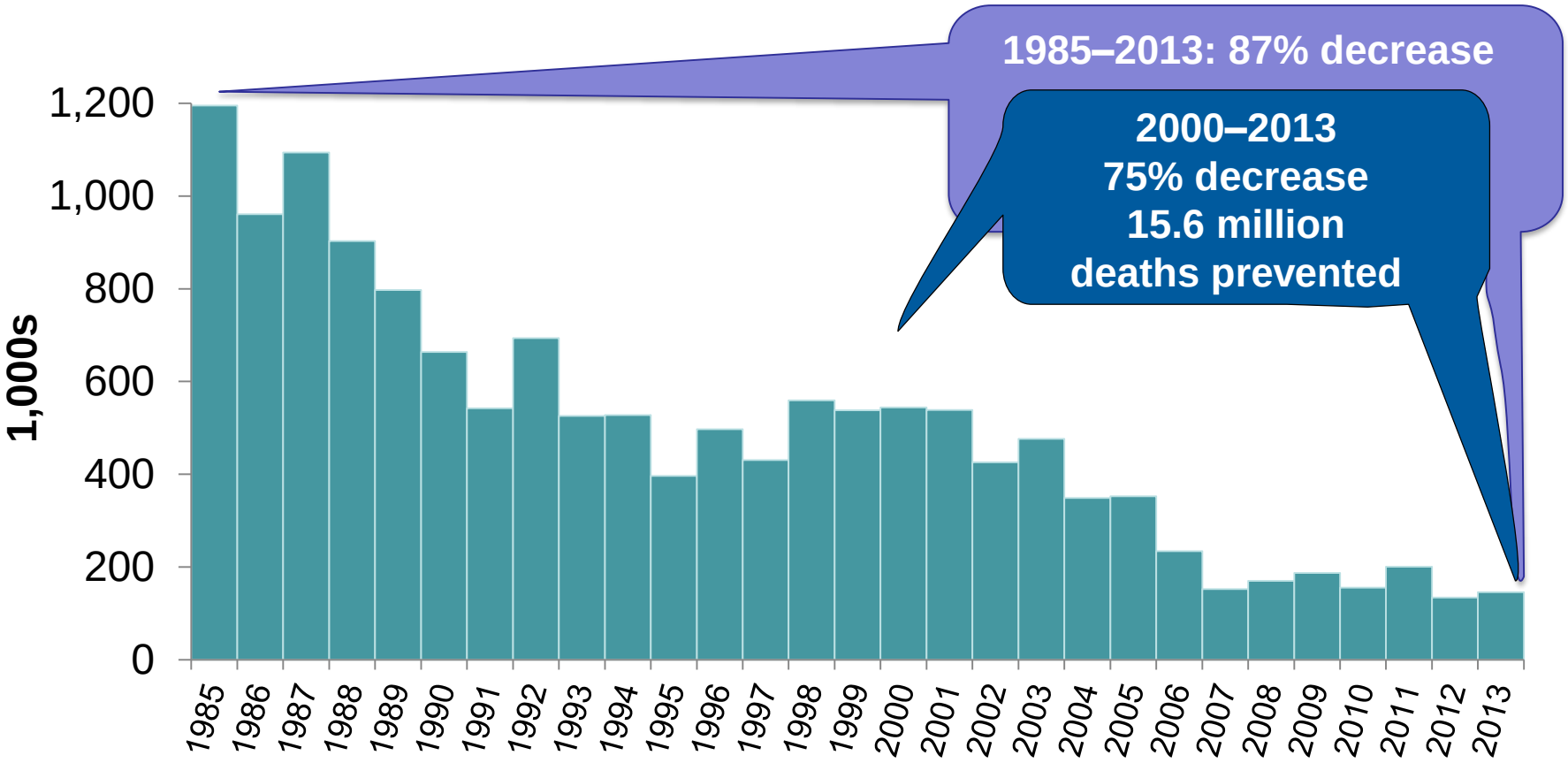
Integrated interventions:

- **OPV – 13**
- **Vitamin A – 8**
- **De-worming – 5**
- **Bed nets or other – 2**

SIA: Supplemental immunization activities
OPV: Oral polio vaccine
Immunization Vaccines and Biologicals, WHO, as of May 25, 2015

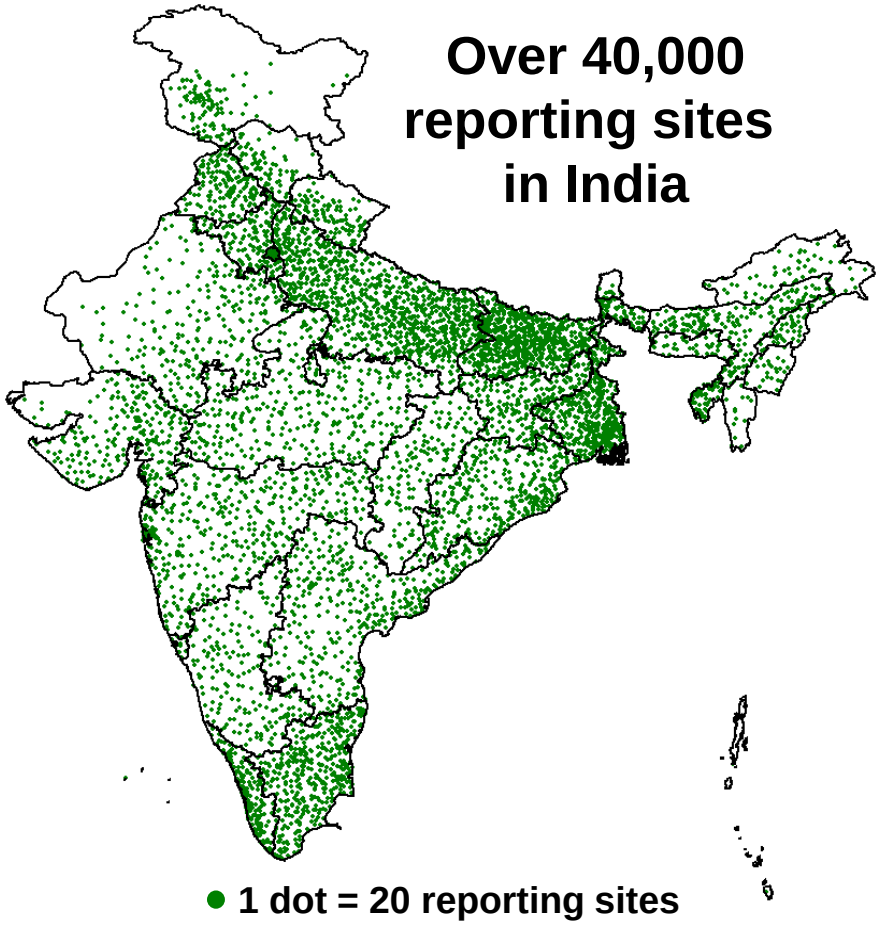
Reduction in Estimated Measles Deaths, 1985–2013

2015 Global Target: Measles mortality reduction of 95% vs. 2000 estimates



MMWR 2014;63:1034-8

India Retooling to Eliminate Measles and Rubella



- Strong political commitment
- Polio sites switching to laboratory-supported measles surveillance
- In 2010–2011, measles SIAs reached 119 million children
- In 2016–2018, nationwide MR SIAs will reach 450 million children under 15 years of age

SIA: Supplemental immunization activity
MR: Measles and rubella

Incorporating Lessons and Infrastructure from Polio Eradication Efforts

- **Build on existing infrastructure and investments**
- **Build on knowledge gained through polio eradication efforts**
  - Adapt to areas of insecurity
- **Sustain political leadership and field worker motivation**
  - Use innovative strategies
- **Ensure management capacity and program accountability**
- **Sustain gains to continue improving routine EPI**

Supporting What Works to Eliminate Measles and Rubella

- Secure long-term funding (global and national)
- Engage communities to reach the underserved
- Strengthen routine immunizations
- Integrate surveillance
- Refine strategies through innovation

We Are Working Towards A World Without Measles!

The Role of the Global Measles and Rubella Laboratory Network

Paul A. Rota, PhD

Measles Team Lead,

Measles, Mumps, Rubella, Herpesviruses Laboratory Branch,
Division of Viral Diseases,

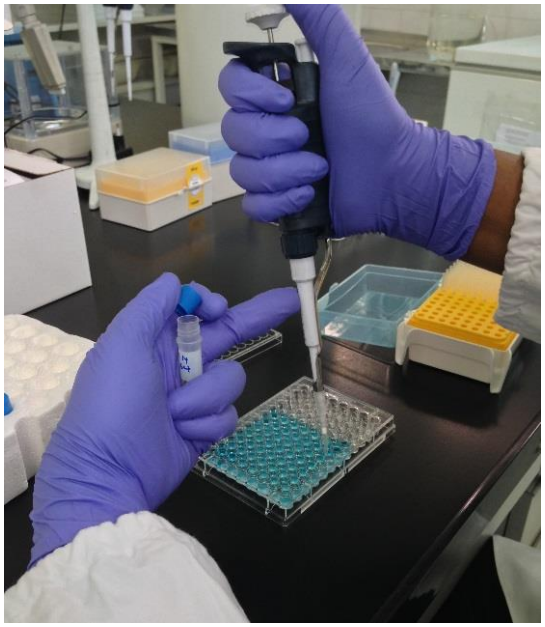
National Center for Immunization and Respiratory Diseases

Laboratory Surveillance for Measles and Rubella Elimination

- Competent and sustainable laboratory support for global surveillance
- Provided by the WHO Global Measles and Rubella Laboratory Network (GMRLN)

Global Measles and Rubella Laboratory Network (GMRLN)

- **Initiated in 2000**
- **Built on Global Polio Laboratory Network model**
- **Multi-tiered structure**
  - 3 Global Specialized Laboratories
    - CDC, PHE-UK, NIID-Japan
  - 14 Regional Reference Laboratories
  - 161 National Laboratories
    - 586 Subnational laboratories (including 362 subnational laboratories in China)
- **7 Global/Regional Laboratory Coordinators**



Dr. M Mulders, WHO Headquarters

Strengths of the GMRLN

- **Standardized testing and reporting structure**
- **Excellent quality control**
- **Timely results that drive public health decision making**
- **Alignment with national public health priorities**
- **Local lab management and control**
- **Integrated testing includes other vaccine preventable diseases**
  - Measles, rubella, Yellow fever, Japanese encephalitis, rotavirus and hepatitis B

Roles of the GMRLN

- Confirm cases of suspected measles or rubella
- Determine genetic relationships of circulating strains
- Measure population immunity

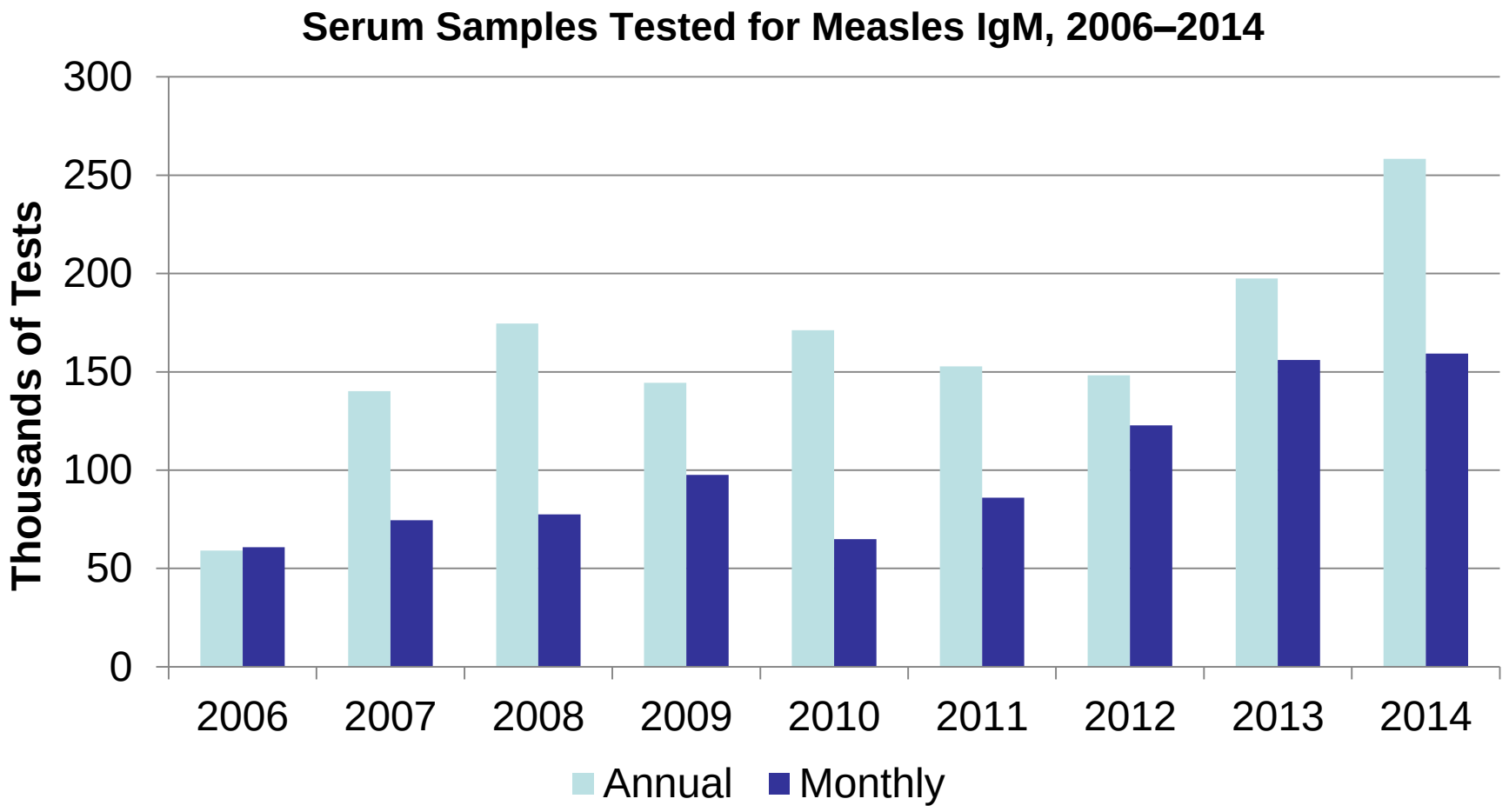
Dr. M Mulders, WHO Headquarters

Laboratory Confirmation of Suspected Measles Cases

- Distinguish measles and rubella cases from other febrile rash illnesses
- Detection of measles or rubella specific IgM in a serum sample taken at first contact with patient
- Detection of viral RNA by RT-PCR

IgM: Immunoglobulin M
RT-PCR: Real time polymerase chain reaction

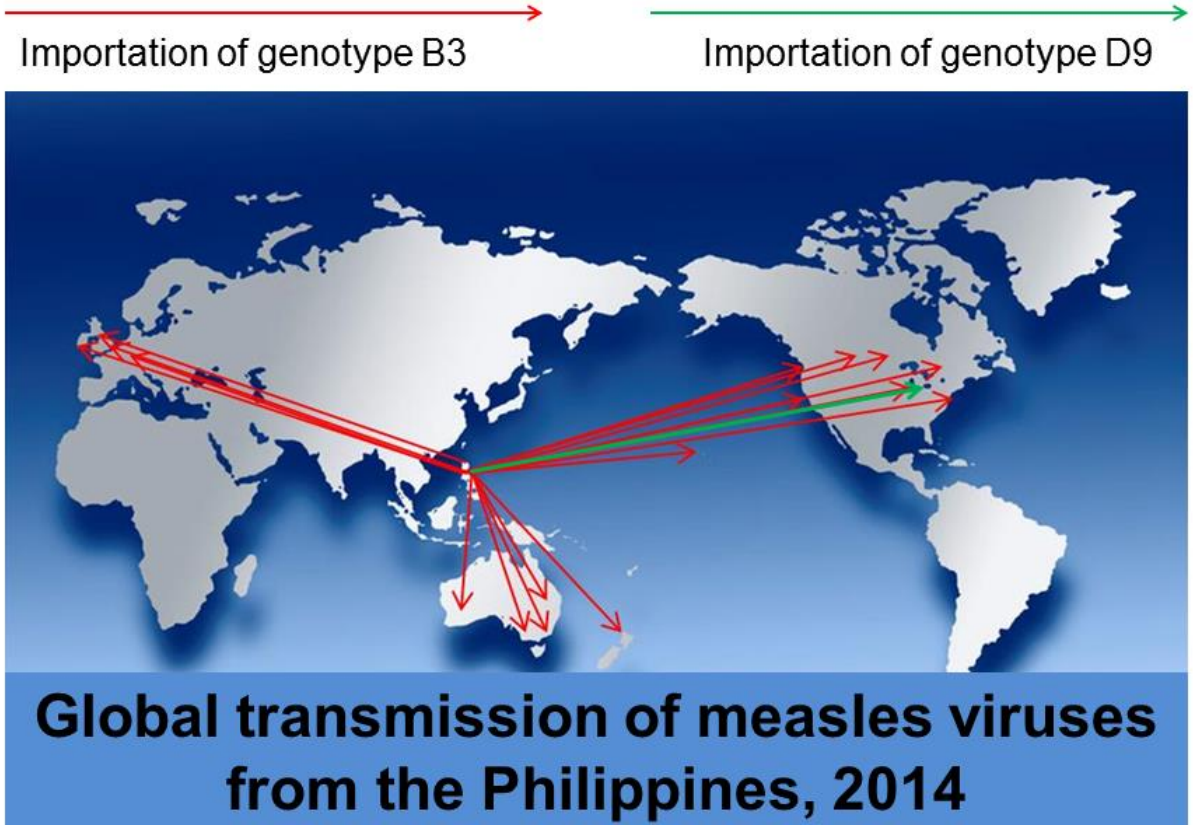
Increasing Workload of the GMRLN



Dr. M Mulders, WHO Headquarters

Genetic Characterization of Measles Viruses to Track Transmission

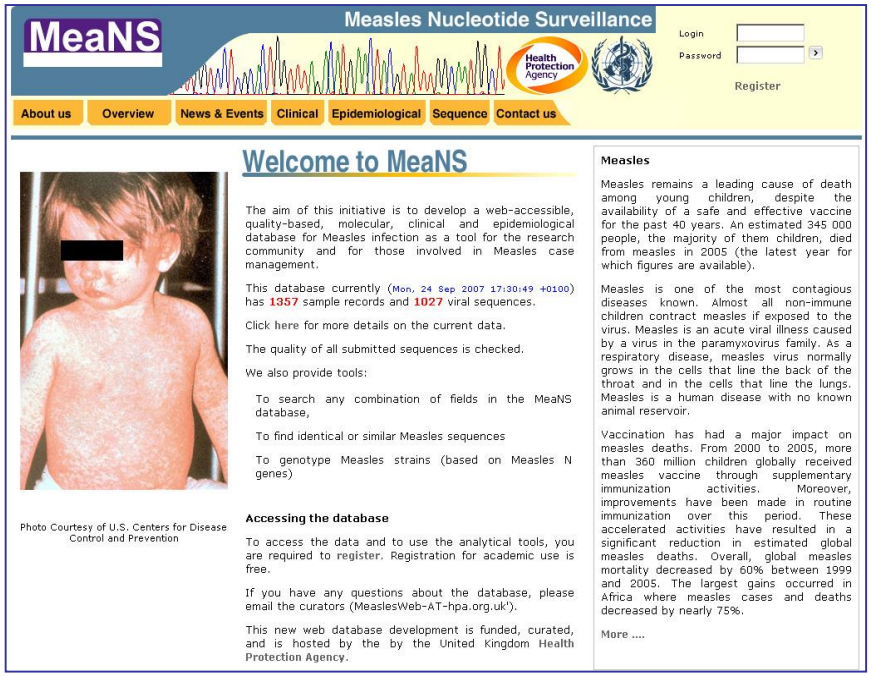
Map transmission pathways and document interruption of transmission



CDC and WHO GMRLN

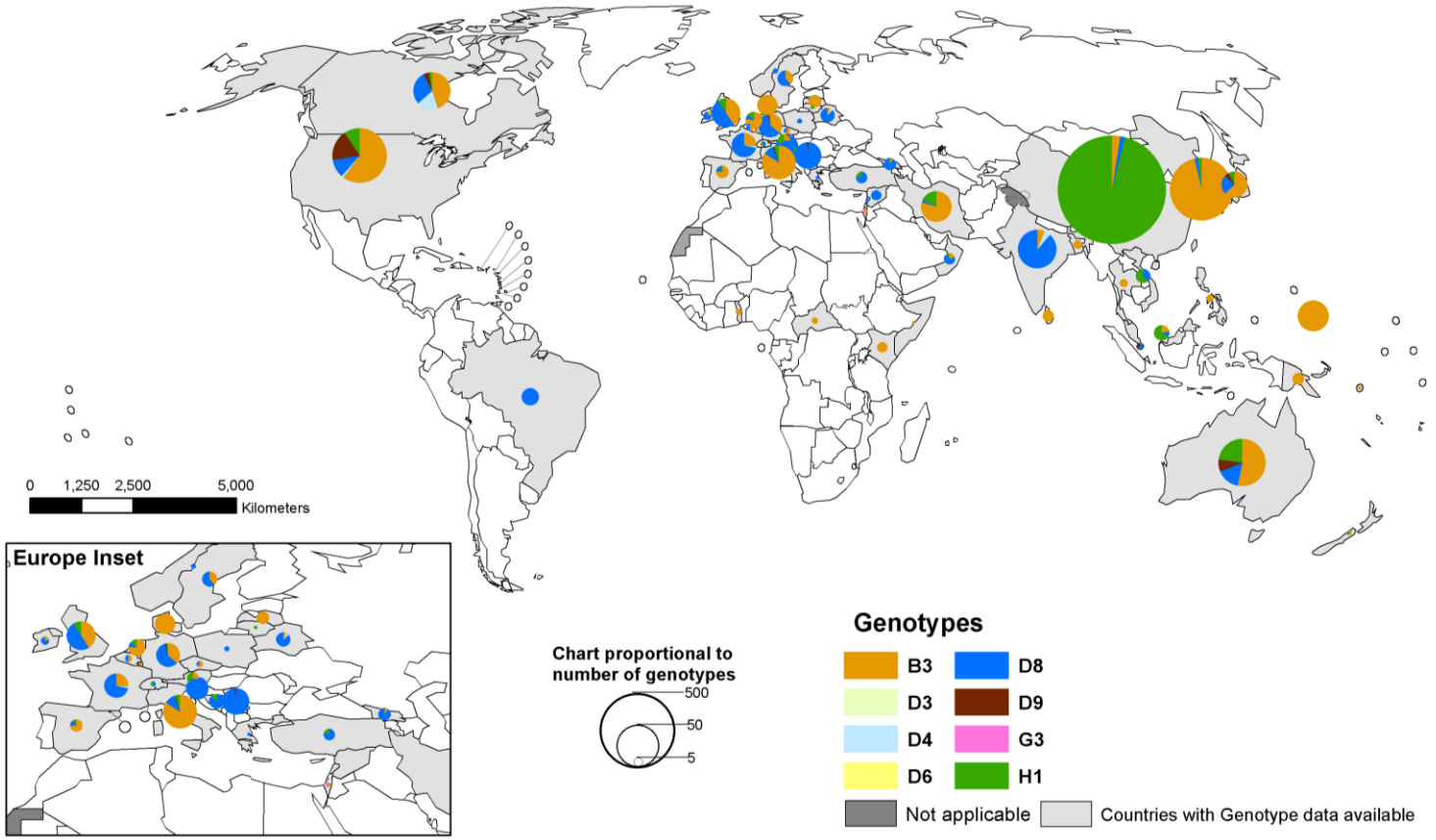
Measles Nucleotide Surveillance (MeaNS)

- **Global genetic sequence database for measles**
- **Maintained at Public Health England**
- **Governance from labs in all WHO regions**
- **Over 22,000 sequences in database**
  - Available to participating labs
  - Discussion of open sharing
- **Rapid sequence analysis and strain detection**



MeaNS Provides Summaries of the Global Distribution of Measles Genotypes

Distribution of measles genotypes: Mar 2014 to Feb 2015



WHO and MeaNS

Confirming Vaccination Coverage

- **Laboratories perform seroprevalence studies to verify vaccination coverage**

CDC, Sue Cho

Challenges for the GMRLN

- Financial sustainability
- Laboratory network expansion (e.g., India)
- Introduction of new laboratory methods
- Sustain and expand quality control program
- Integration with surveillance for VPDs
- Development of effective test strategies for low incidence settings
- Increased workload with national and regional verification of measles elimination

VPD: Vaccine preventable disease

New Technologies on the Horizon

- **New or improved serologic testing methods and assays**
  - High throughput neutralization
  - High throughput seroprevalence
  - Point-of-Care (WHO, PHE)
- **New or improved molecular assays**
  - Whole genome sequencing
  - Next generation sequencing (AMD)
- **Vaccine development**
  - Microneedle patches (GA Tech)

PHE: Public health, environmental and social determinants of health, WHO
AMD: Advanced Molecular Detection, CDC
GA Tech: Georgia Institute of Technology

Thanks to the GMRLN and Measles and Rubella Teams at CDC

12th Annual Global Measles and Rubella Laboratory Network Meeting, September 2014, Istanbul, Turkey

The Elimination of Measles in the Americas

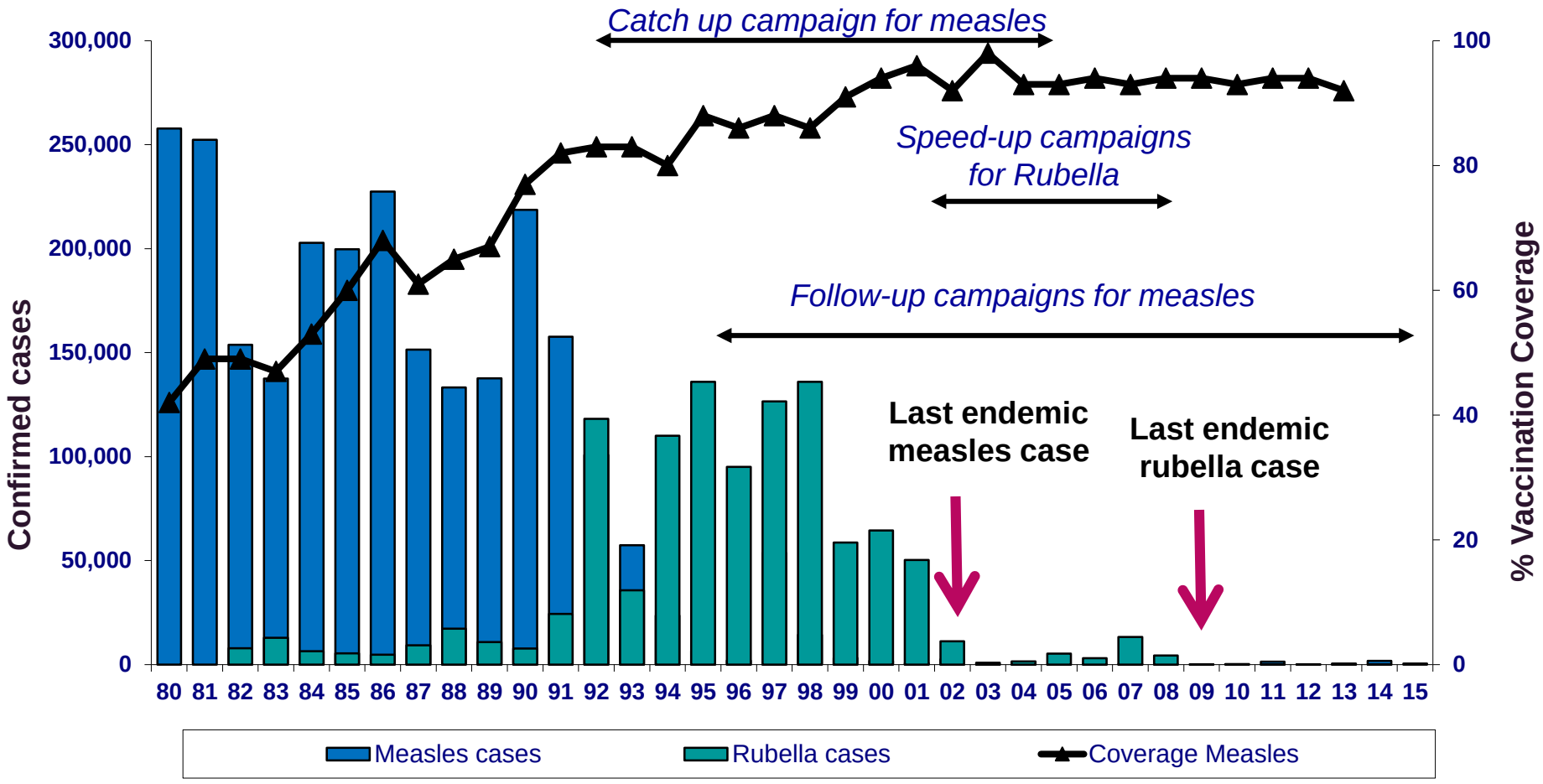
Desirée Pastor, MD, MPH
Regional Immunization Advisor
Pan American Health Organization
Regional Offices for the Americas, World Health Organization

Outline

1 **Update of measles epidemiology in the Americas**

2 **Most critical challenges for sustaining the gains**

Impact of Measles and Rubella Elimination Strategies in the Americas

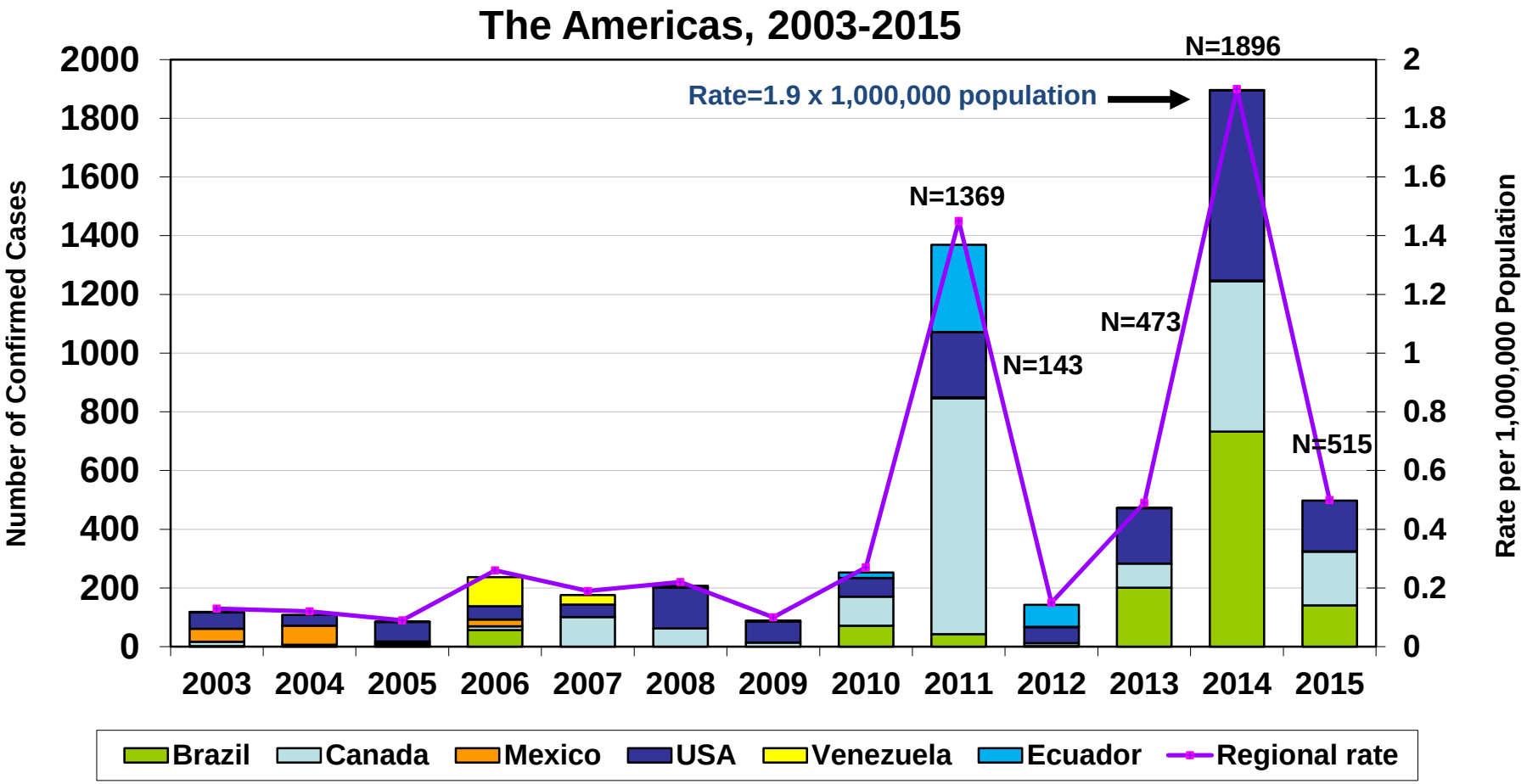


The Comprehensive Family Immunization Unit (FGL/IM) – Pan American Health Organization, data as of June 8, 2015

Pan American Health Organization

World Health Organization Americas

Distribution of Confirmed Measles Cases After Interruption of Endemic Transmission



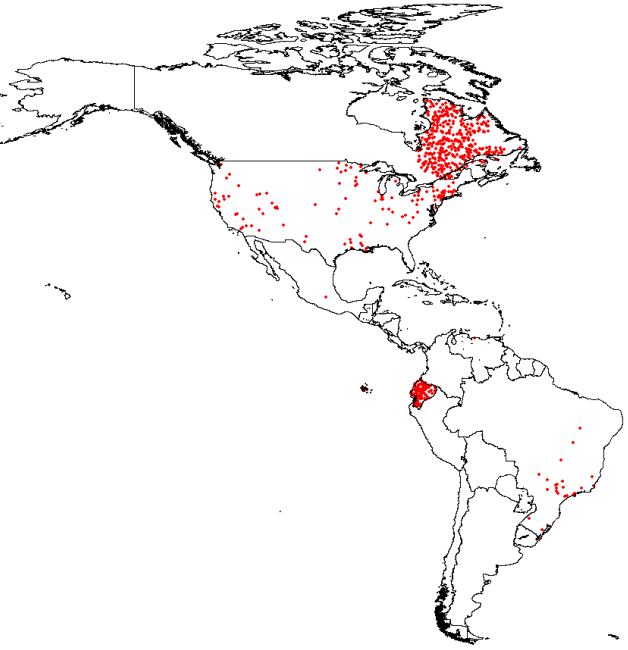
PAHO Measles Eradication Surveillance System and Integrated Surveillance Information System and country reports to The Comprehensive Family Immunization Unit (FGL/IM) – Pan American Health Organization, as of epidemiological week 21, 2015

Pan American Health Organization

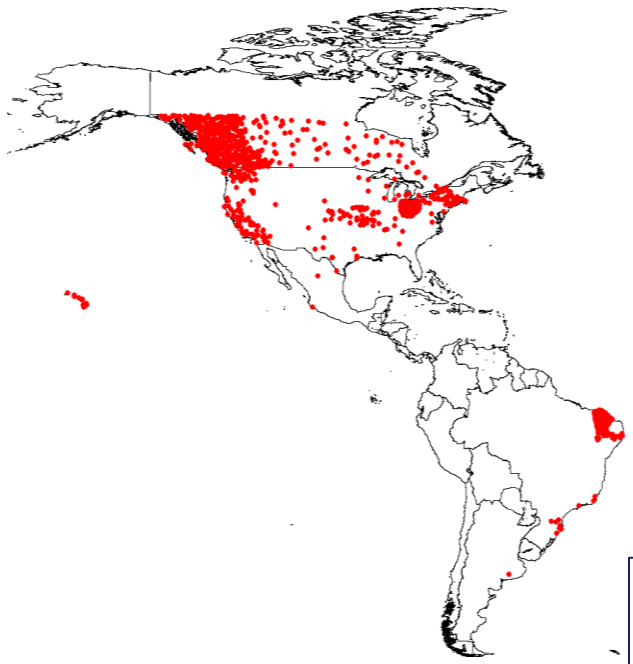
World Health Organization Americas

Geographic Distribution of Confirmed Measles Cases In The Americas

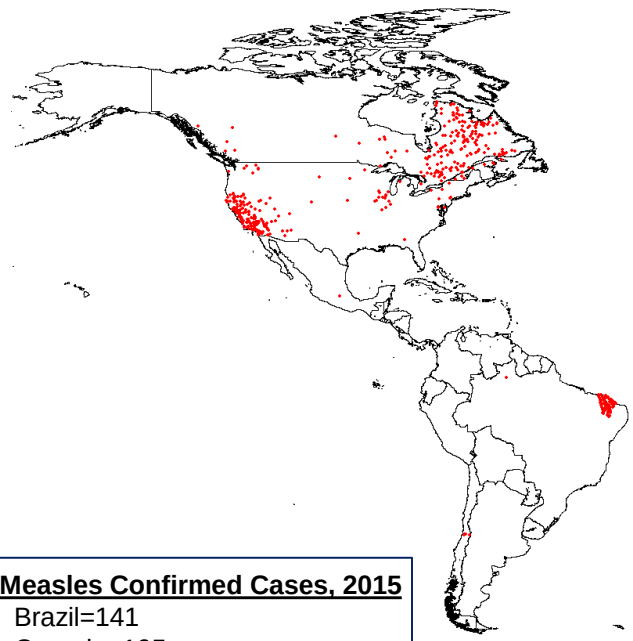
2011
N=1,369 cases



2014
N=1,896 cases



2015* to date
N=515 cases



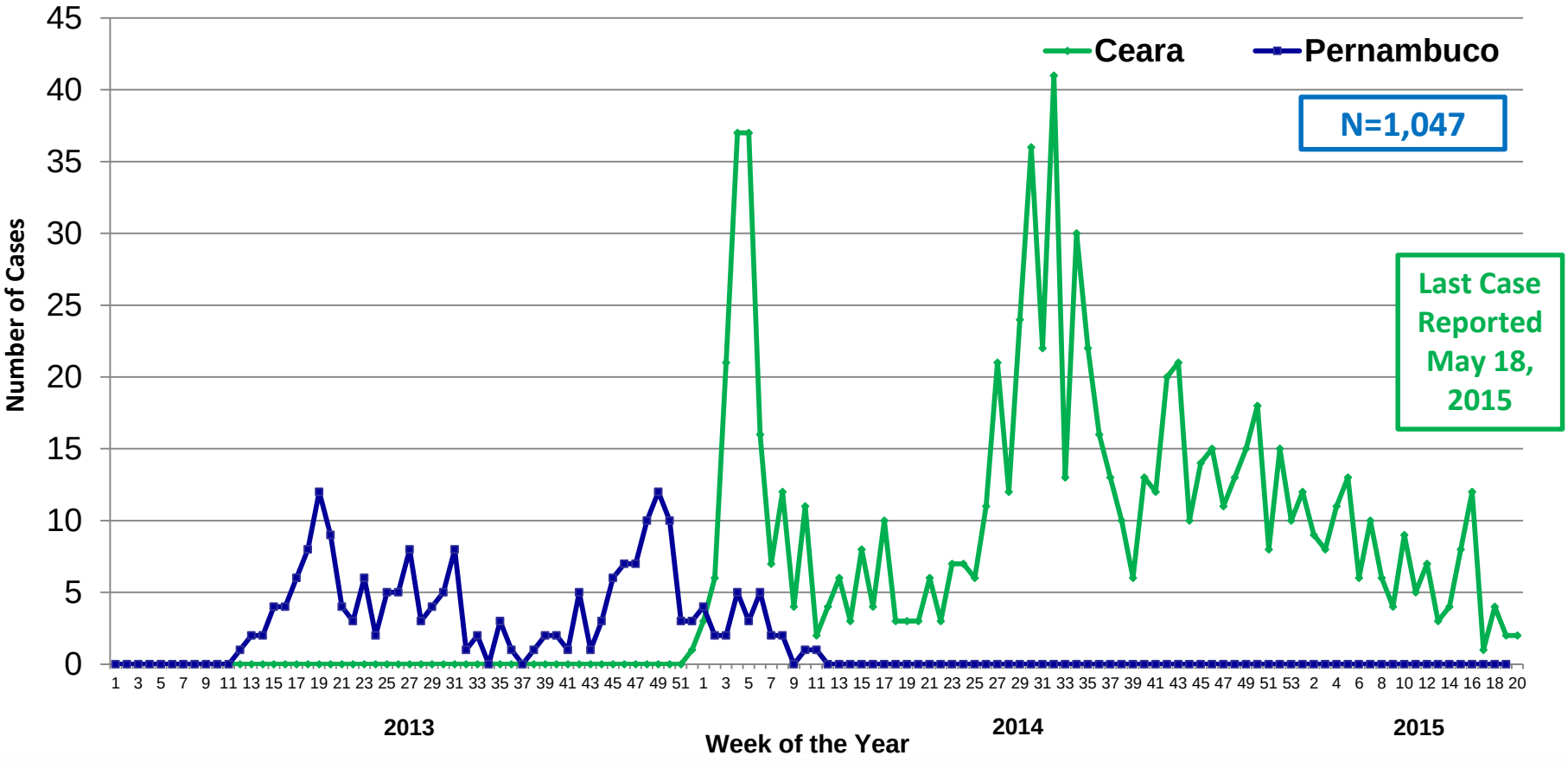
1 red dot = 1 measles case

Measles Confirmed Cases, 2015
Brazil=141
Canada=195
Chile=5
Mexico=1
USA=173
Total= 515 cases

The Comprehensive Family Immunization Unit (FGL/IM) – Pan American Health Organization, as of epidemiological week 21, 2015 by second administrative level

First Outbreak in Post Elimination Era with More Than 12 Months of Transmission

Confirmed Measles Cases by Epidemiological Week, Selected States Brazil, 2013-2015



The Comprehensive Family Immunization Unit (FGL/IM) – Pan American Health Organization, as of June 8, 2015epidemiological week 21, 2015 by second administrative level

Characteristics of Measles Outbreaks in the Americas

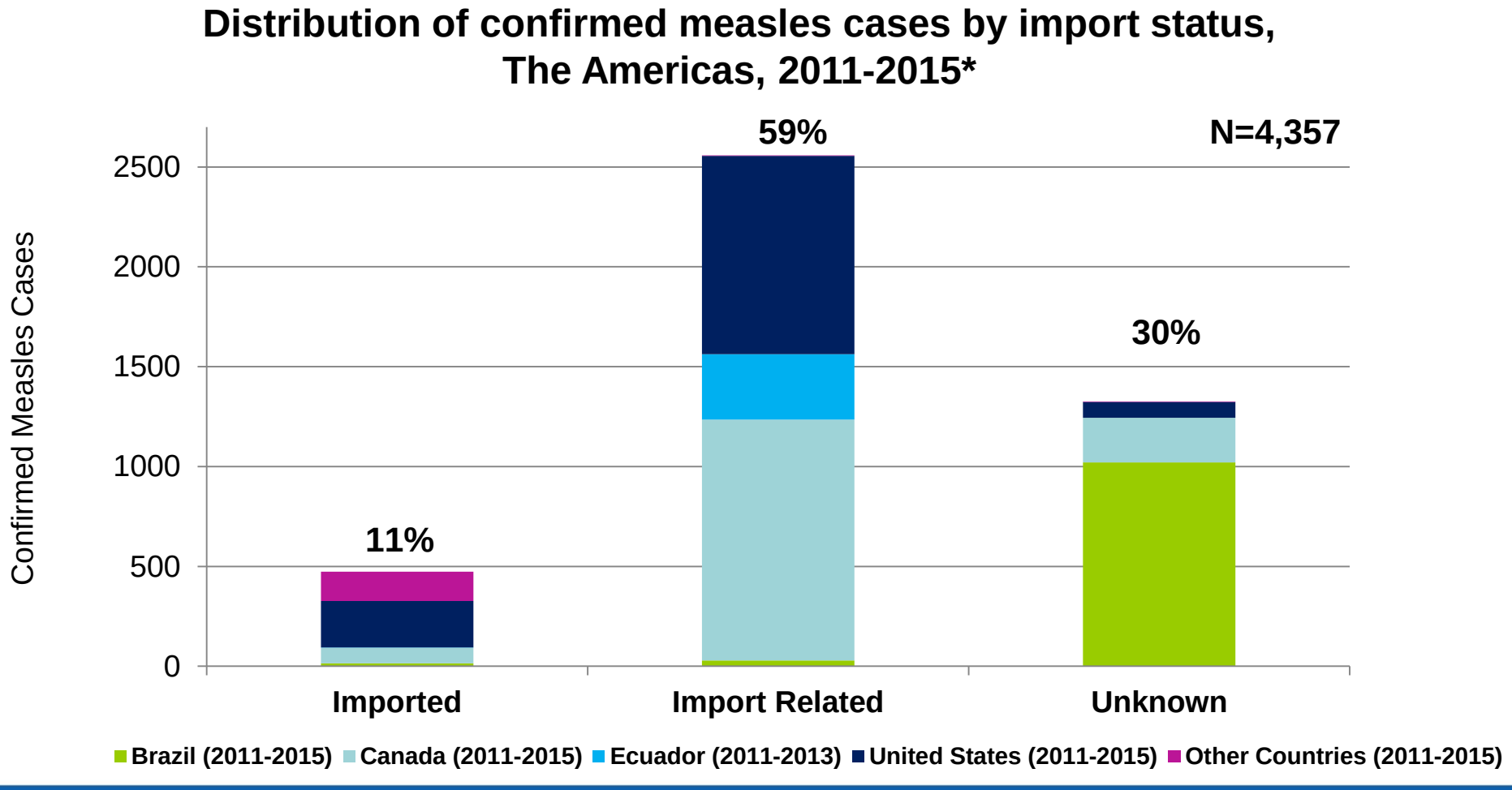
	USA (2014–2015)	Brazil (2013–2015)
Spread	Rapid spread within US and neighboring countries (Canada, Mexico)	Slow, sustained spread with 'drop by drop' transmission in Pernambuco and Ceará
Genotype	More than one genotype in US and Canada	Single genotype, one outbreak
Outbreak Control	Rapidly controlled	Ongoing outbreak after 24 months
Ages of Cases	USA: 53% 5–39y and 28% in <5y	Pernambuco: 48% <1y Ceará: 28% <1y and 34% 15–29y
Case Vaccine Status	More than 80% unvaccinated	Around 89% unvaccinated
Barriers to Vaccination	Philosophical or religious exemptions, or too young to vaccinate	Non-eligible for vaccine, limited access to health services, lack of vaccines, limited human resources

Outline

1 **Update of measles epidemiology in the Americas**

2 **Most critical challenges for sustaining the gains**

Imported Cases Are Biggest Threat to Maintaining Elimination Efforts



PAHO Measles Eradication Surveillance System and Integrated Surveillance Information System and country reports
*Data as of 21 May 2015

Pan American Health Organization
World Health Organization
Regional Office for the Americas

Recommendations to Any Person Traveling to Areas with Measles Circulation

PAHO recommends that any traveler over the age of six months be fully vaccinated against measles and rubella, at least 2 weeks before departure.

For the duration of the trip and upon returning, travelers should note any of the following symptoms:

- Fever
- Rash
- Cough, coryza (runny nose), or conjunctivitis (red eyes)
- Joint pain
- Lymphadenopathy (swollen glands)

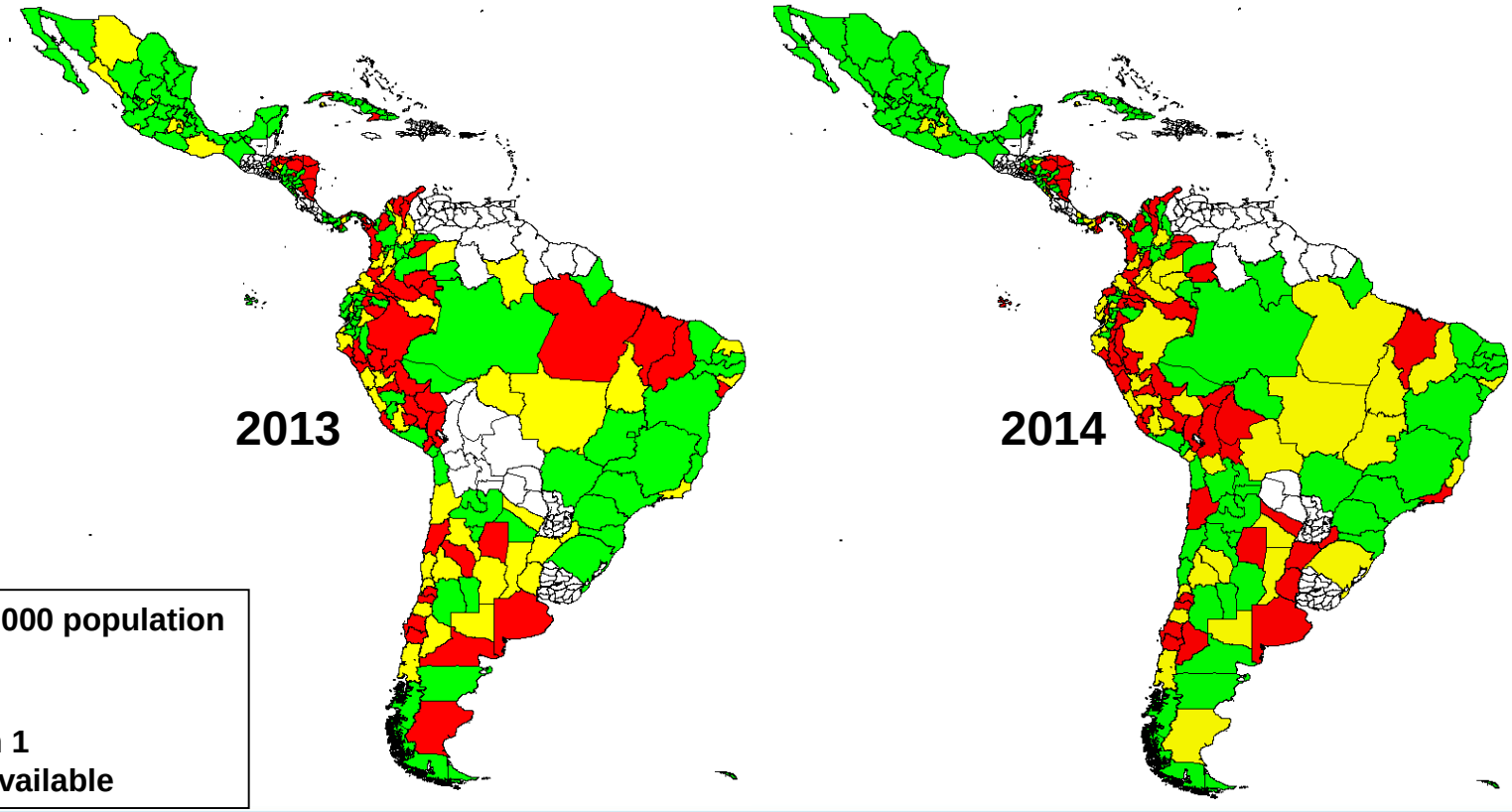
If travelers suspect they have measles or rubella, they should:

- Remain at their current residence (e.g., hotel or home) except to seek professional health care.
- They should not travel nor go to public places.
- Avoid close contact with other people for seven days following onset of rash.

Ensuring Quality of Surveillance at the Subnational Level

Rate of Suspected Measles/Rubella Cases, Sub national Level, 2013-2014

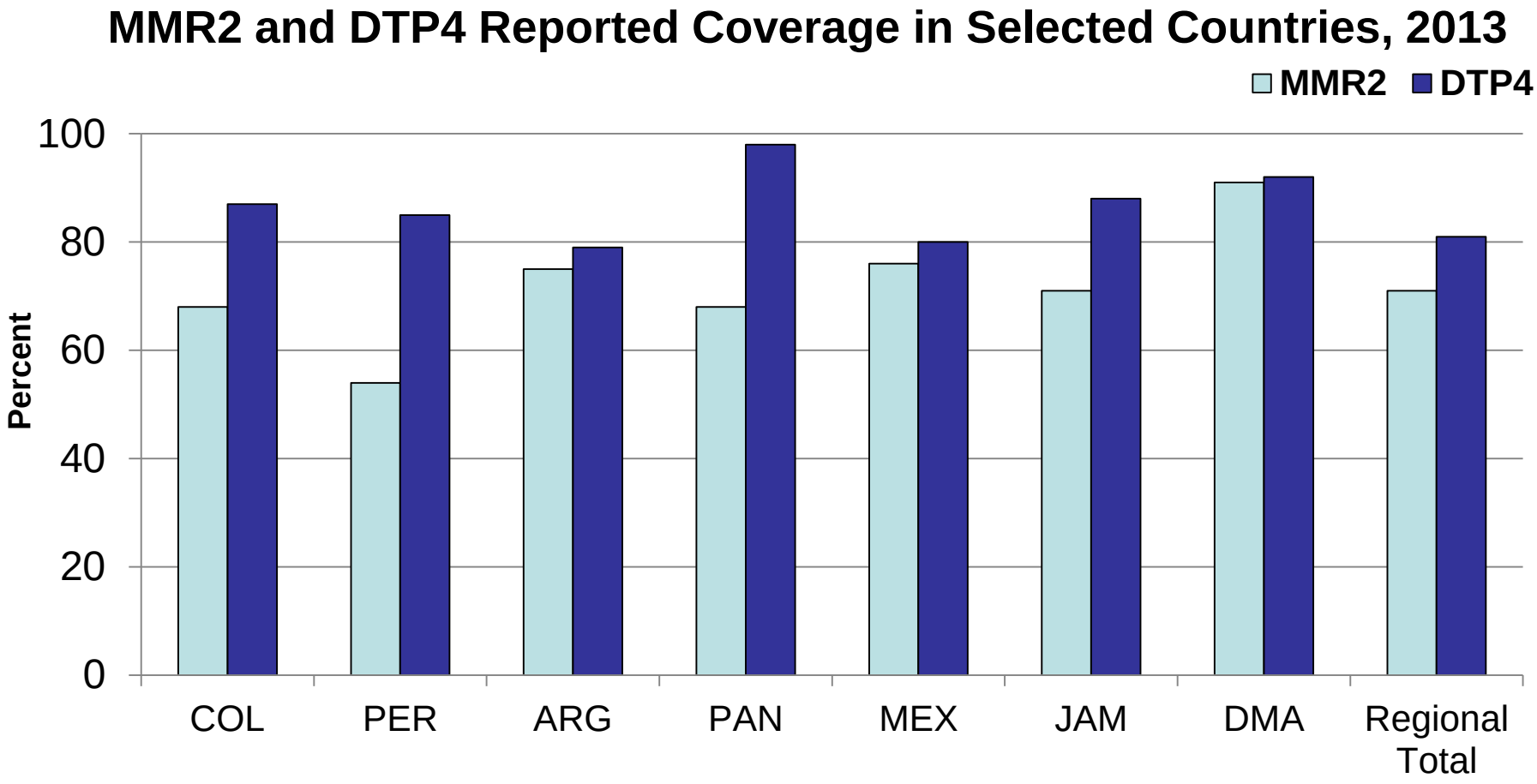
Expected rate is 2 or more per 100,000 population



The Comprehensive Family Immunization Unit (FGL/IM) – Pan American Health Organization

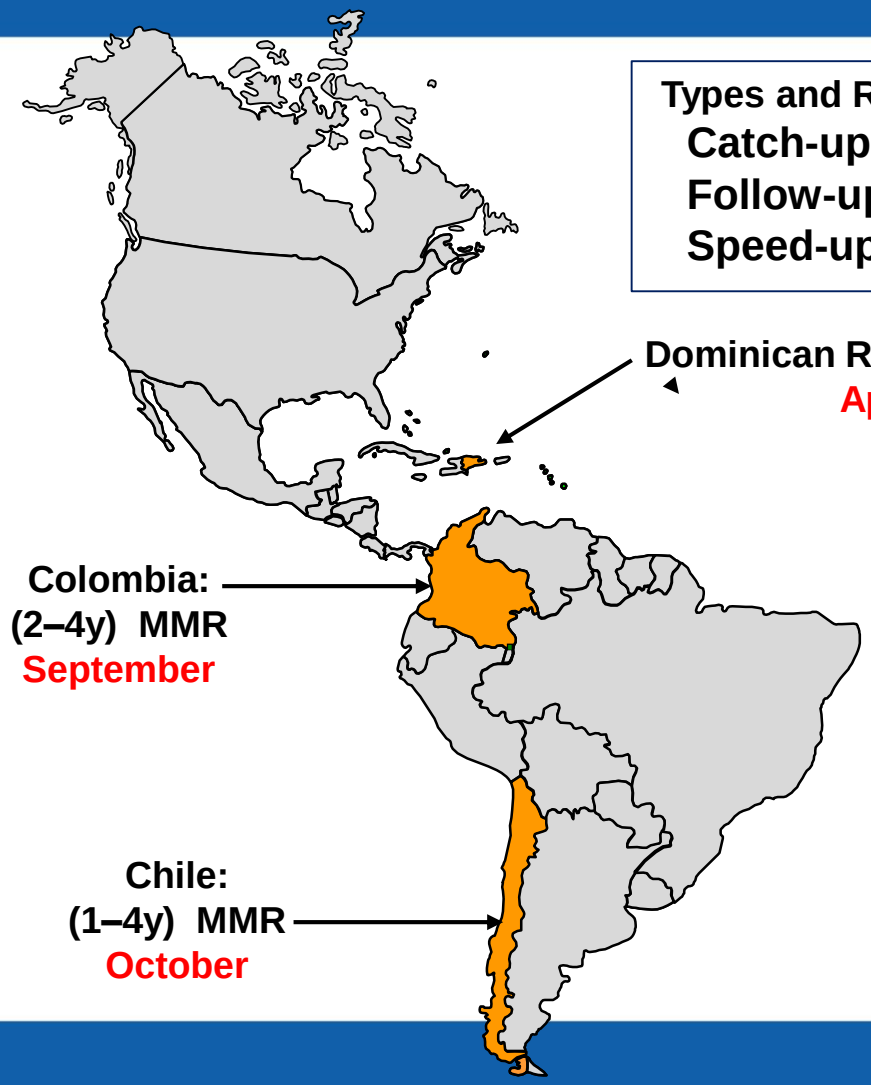
Pan American Health Organization
World Health Organization
Americas

Overcoming Immunity Gaps by Giving MMR2 and DTP4 Simultaneously



MMR2: Measles, mumps and rubella, second dose DTP4: Diphtheria, tetanus and pertussis, fourth dose
COL: Colombia PER: Peru ARG: Argentina PAN: Panama MEX: Mexico JAM: Jamaica DMA: Dominican Republic
PAHO-WHO/UNICEF Joint Reporting Form, 2014

Ensuring Second Vaccination Opportunity To Maintain Measles and Rubella Elimination



Types and Reach of Mass Vaccination Campaigns

Catch-up (<15y): 140 million persons
Follow-up (1–4y): 60 million children
Speed-up (adol/adult): 250 million persons

Programmed Follow-up Campaigns in the Americas, 2105

Adol: Adolescents

The Comprehensive Family Immunization Unit (FGL/IM) – Pan American Health Organization, as of June 11, 2015

Challenges to Sustain the Gains

- Increase quality of MR surveillance indicators to rapidly respond to imported MR cases
- Increase data analysis at the local level for strengthening MR surveillance
- Increase MMR1 and MMR2 vaccination coverage
- Support countries to ensure high quality follow-up campaigns
- Declare measles eliminated in the Americas by 2016

Email: immunization@paho.org
Web: www.paho.org/immunization

Global Strategy to Eliminate Measles

Peter Strebel, MBChB, MPH
Accelerated Disease Control Leader
Expanded Programme on Immunization
World Health Organization

World Health Organization

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

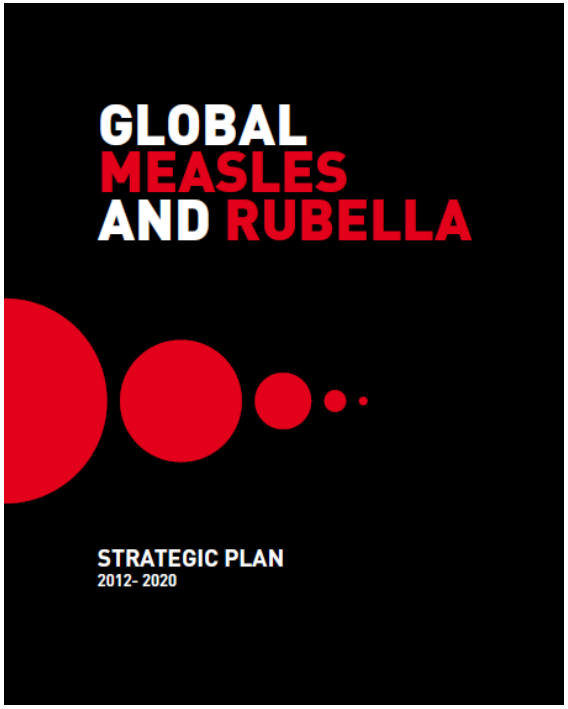
Outline

- What are the strategies?
- Why has progress slowed?
- How can progress be accelerated?

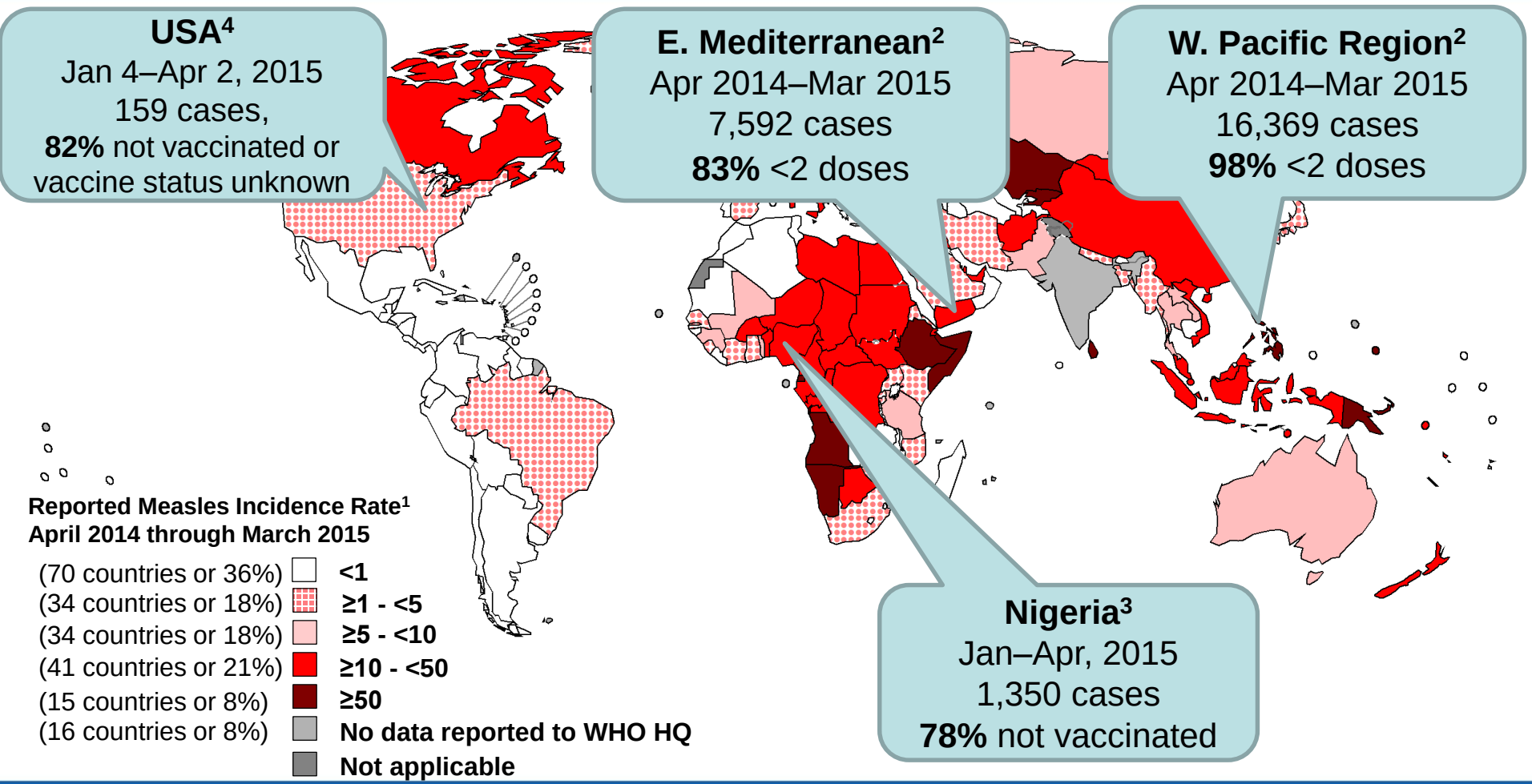
Global Measles and Rubella Strategic Plan

5 Key Strategies:

1. Achieve high population immunity through vaccination
2. Conduct effective surveillance and monitoring
3. Develop outbreak preparedness and response
4. Communicate to engage public's confidence and build demand
5. Perform research and development to improve program efficiency

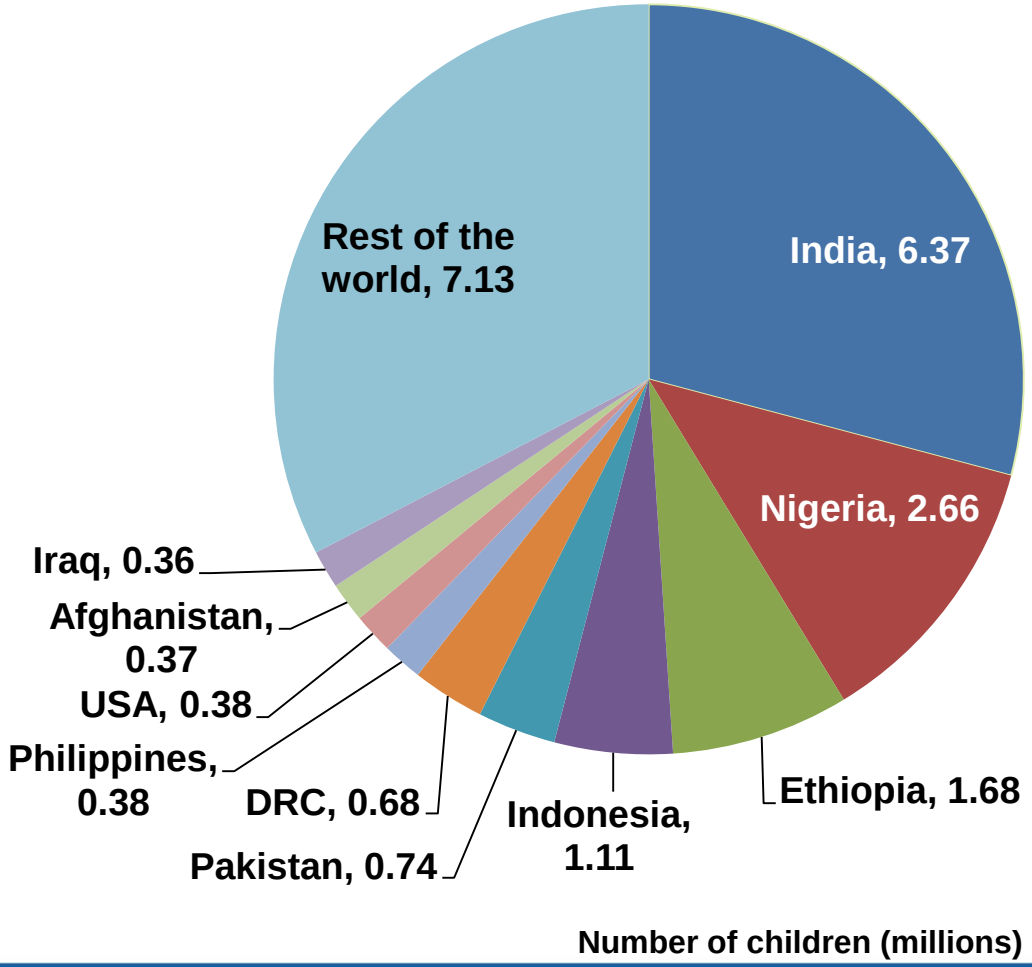


Failure to Vaccinate Causes Measles Outbreaks



1. Rate per 1,000,000 population
2. WHO/HQ monthly measles surveillance data as of May 4, 2015
3. WHO/African Region measles surveillance data as of May 14, 2015
4. MMWR April 2015:64;373-376

21 Million Infants Missed MCV1 in 2013



- **Over 60% of these children are in 6 countries**
  - **India**
  - **Nigeria**
  - **Ethiopia**
  - **Indonesia**
  - **Pakistan**
  - **Democratic Republic of Congo (DRC)**

Global Routine Immunization Strategies and Practices – A Call to Invest in 8 Core Areas

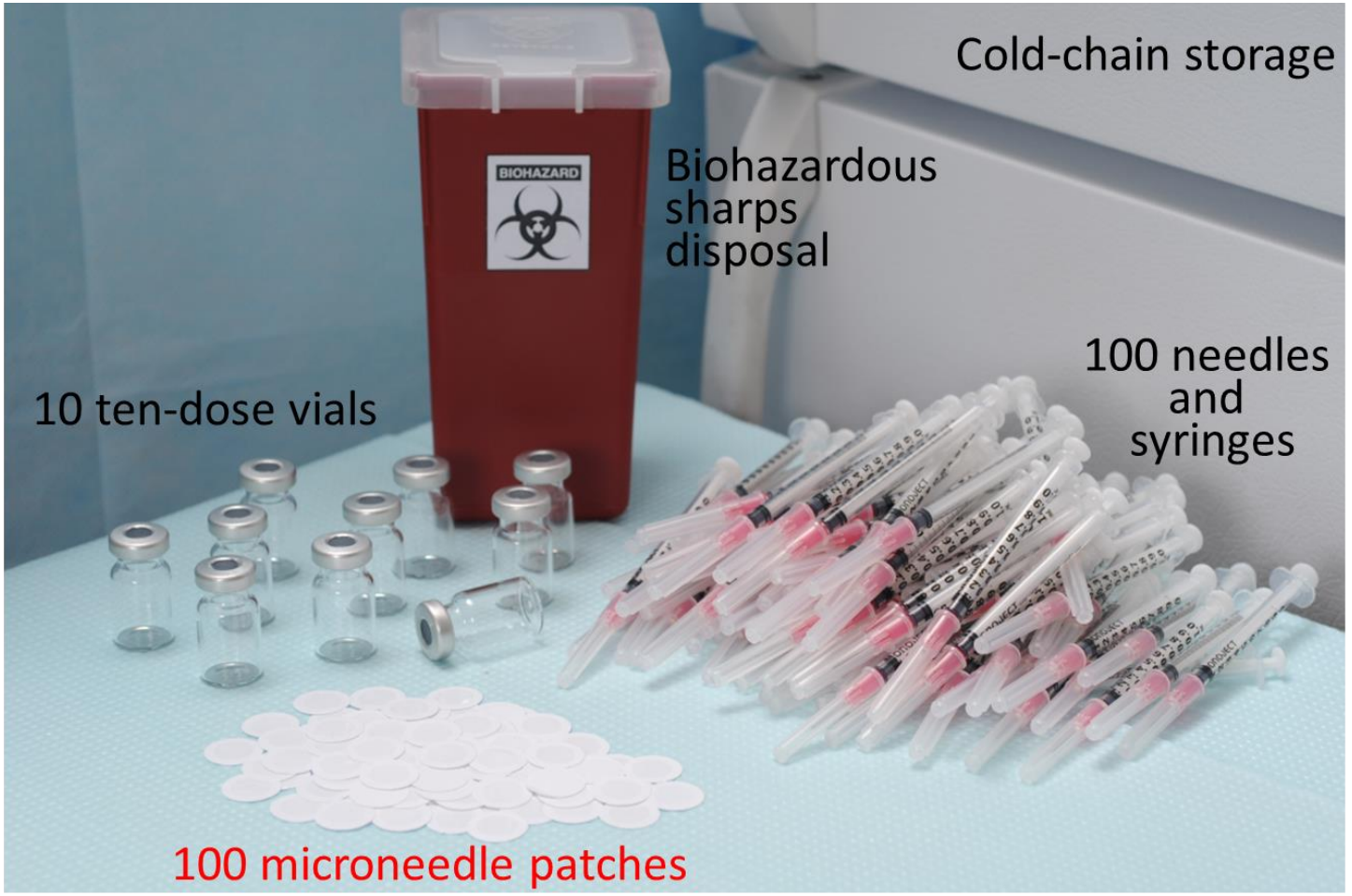
Global Routine Immunization Strategies and Practices (GRISP),
a companion document to the Global Vaccine Action Plan (GVAP), DRAFT June 10, 2015

Monitoring Progress through Regional Verification of Measles Elimination, 2014–2015

WHO Region	Regional Verification Commissions Established	Elimination Achieved	
		No. of countries	% of countries
Americas[1]	Yes	34	97%
Europe[2]	Yes	22	41%
Western Pacific[3]	Yes	6	22%
Eastern Mediterranean	No	-	-
South-East Asia	No	-	-
Africa	No	-	-

1. Progress report on Plan of Action for Maintaining Measles, Rubella, and CRS Elimination in the Americas, September 12, 2014
2. Third meeting of the European Regional Verification Commission for Measles and Rubella Elimination (RVC) November 2014
3. http://www.wpro.who.int/mediacentre/releases/2015/20150327/en/

Innovations – Intradermal Patch Vaccination



GA Tech and CDC

Measles and Rubella Initiative Management Team

Strategies

1. Achieve and maintain high levels of population immunity
2. Communicate and engage to build public confidence
3. Monitor disease using effective surveillance
4. Maintain outbreak preparedness and response
5. Research and develop improved vaccination & diagnostic tools

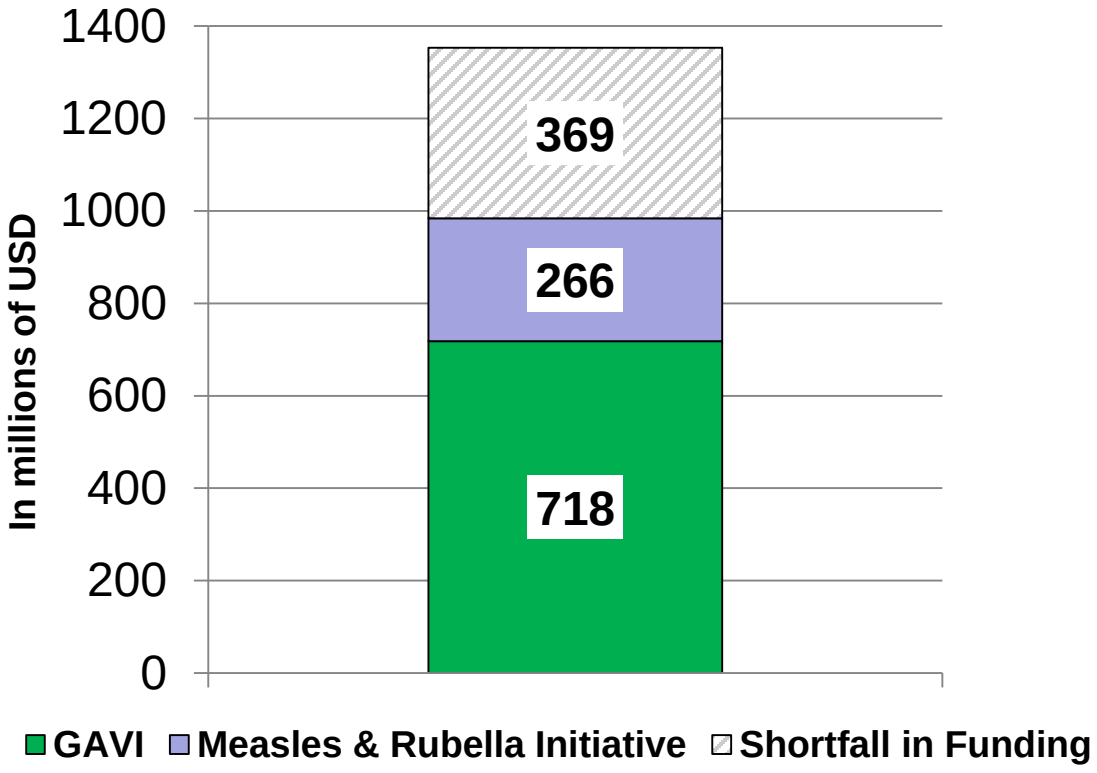
Working Groups

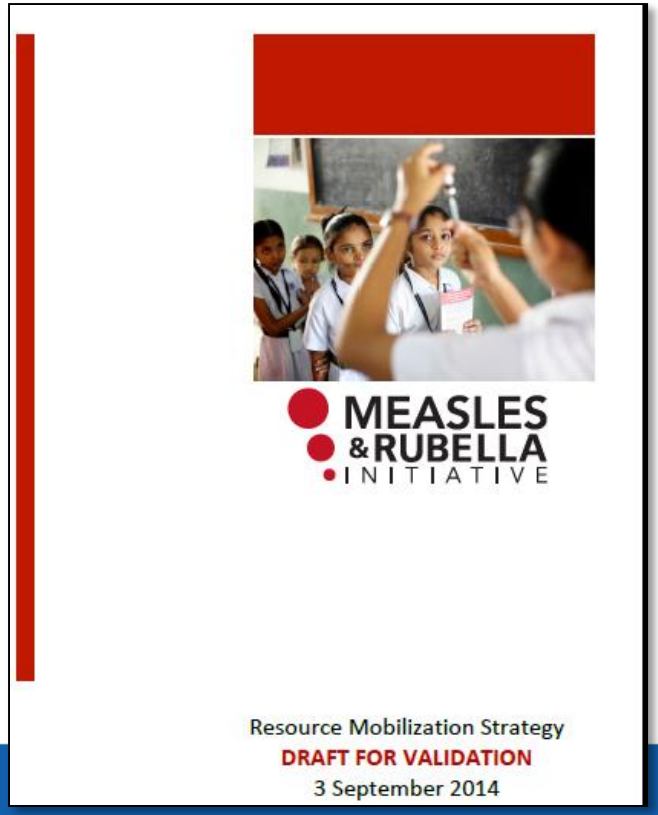
- Resource Mobilization
- Routine Immunization
- Strategic Communications
- Programme Implementation
- Vaccine Supply Coordination
- Research and Innovation

2013 Annual Report of the Measles and Rubella Initiative
http://www.measlesrubellainitiative.org/wp-content/uploads/2014/08/annual-report_2014.pdf

Critical Shortfall of Funding

$1.4 billion needed for measles and rubella control, 2015-2020





Implementing Our Plan

- **5 clear strategies to eliminate measles and rubella**
- **Cause of recent outbreaks is failure to fully implement the strategies**
- **To accelerate progress we need**
  - Investment in immunization programs
  - Verification commissions to monitor progress
  - Game-changing solutions
  - Effective program management
  - Resource mobilization

Regaining Momentum in the Fight Against Measles

- **Measles is preventable through vaccination**
- **Combined vaccines make it possible to eliminate rubella and measles**
  - The Region of the Americas eliminated rubella in April 2015
- **The Global Measles and Rubella Laboratory Network provides valuable surveillance and disease tracking**
- **Progress has slowed and gains in some regions have been lost**
- **"The best defense against measles is a strong offense."**

  –Walt Orenstein

Orenstein, WA and Seib K. NEJM, 2014

Thank You

Achieving a world without measles by connecting the dots